

How to Help with Protein

THE prospect of world-wide famine, always something of a scarecrow, has been diminished in the past few years by the increased production of cereals in many developing countries, but—quite properly—that has merely served to concentrate attention on the intractable nutritional problems which are certain to outlast the threat of mere hunger. Indeed, there are in some parts of the world theoretical dangers that the green revolution as it is called will intensify the problems of protein deficiency, partly because an adequacy of calories will make it possible for larger numbers of people to survive to suffer the overt symptoms of protein deficiency—kwashiorkor, for example—and partly because excitement about cereals may divert attention from crops such as peas and beans which contain more protein than wheat or rice. In the circumstances, much might have been expected of the eighth report of the joint FAO and WHO Expert Committee on Nutrition, which deals with two important aspects of the problem, the fortification of food with supplements, artificial and otherwise, and with the precise definition of protein-calorie malnutrition (World Health Organization, Technical Report Series Number 147, HMSO, £0.40). In reality, the document is a disappointment, and the acknowledged complexity of the subject is only partially an excuse.

The prevalence of protein deficiency is, of course, imperfectly defined, even if the estimate some years ago by the FAO that something like 60 per cent of the world's population is malnourished is now seen to be a gloomy upper limit. Part of the trouble is diagnostic. The high death rate in developing countries among children under five, often ascribed to infectious diseases among which measles is conspicuous, is now known to be a sign of malnutrition. How else is it possible to explain that the rate of death among infants in developing countries may be twenty or thirty times that in the United States or Western Europe? But a child who dies from an infection is recorded as a casualty of that disease and not of the malnutrition which may have made him susceptible to it.

This is why the Expert Committee on Nutrition is right to ask for more subtle surveys of the incidence of malnutrition among the young children of developing countries. Often it may be that the best signs are anthropometric—height and weight during infancy are useful indicators of the adequacy of a diet. The committee's report would have been more useful if it had included a review of some of the attempts which have been made in recent years to apply just these criteria to the assessment of the degree of malnourishment in developing countries. There is some evidence that malnourishment of a degree which may be converted into a frank expression of nutritional disease such as kwashiorkor or marasmus (calorie deficiency) is present in between 5 per cent and 45 per cent of the children of developing countries, but plainly there is a great need for more

accurate information before the scale of the problems which must now be tackled can be defined.

Whatever the figures may eventually reveal, there is very little doubt that subclinical malnutrition is a more severe handicap for developing nations than even the alarming incidence of kwashiorkor and marasmus might suggest. Many of the consequences of malnutrition in infancy are, after all, ineradicable. A child with kwashiorkor may survive if he is fed protein in time, but his capacity for mental development may be permanently impaired. Mr Robert McNamara, urging the Governors of the World Bank to a more vigorous programme of assistance in nutrition, put the point vividly last September by declaring that the brains of some malnourished children had been found at autopsy to contain only half the number of cells found in properly nourished children. The importance and the urgency of the problem can be inferred from the dominance of the younger age groups in the populations of developing countries, where roughly 40 per cent of the population is younger than fifteen. It would plainly be intolerable if the nations of the developed world, having helped enormously with the removal of calorie deficiency, were not now to follow with substantial programmes of assistance with the objective of abating malnutrition. Fair play, several agencies, the Ford Foundation and the World Bank conspicuous among them, have now plainly recognized the need for increased effort.

What can be done? It is proper to recognize that simple solutions are often inapplicable or less effective than their first promise would suggest. Schemes for fortifying cereal foods by the addition of protein concentrates of various kinds or even with synthetic amino-acids, lysine for example, are potentially cheap but are often less effective than they might be because of difficulties of distribution. It goes without saying, of course, that uneven distribution of foods containing protein is often the chief cause of protein malnutrition. In India, for example, an estimate by the President's Science Advisory Committee in the report on the "World Food Supply" suggested that even in the early 1960s, the supply of protein amounted to 55.6 grams per day, rather more than the estimated need of 48.3 grams per day. The trouble, of course, is that the foods which contain most protein, and animal protein in particular, are more expensive and therefore less easily accessible to poor people than to the well-to-do. But there are physical as well as financial difficulties in making sure that artificially fortified foods will find their way to the sections of a developing population most in need of them. Paradoxically, some of the countries of south-east Asia, now looking forward to the prospect of self-sufficiency in cereals, may find themselves deprived of the protein supplements which have in recent years been added to exports of grain from North America under the various aid programmes which have been mounted.



The means of fortifying cereal foods are technically simple, but the experience of the past few years has shown that there may be all kinds of difficulties in using them. Several kinds of protein supplements have been used, ranging from the fish protein concentrate obtained by processing fish in bulk to extracts of soya flour. Although the costs of the protein manufactured in ways like these are less than for that from animal products, there are often limits to the extent to which they can be added to grain or flour without impairing cooking quality or taste. The use of lysine as a means of fortifying cereals is predicated on the tendency for most cereal crops to be comparatively impoverished in this essential amino-acid, and the material can be manufactured synthetically even in countries which have not established indigenous chemical industries.

An article in the current issue of the *Harvard Business Review* by Mr Alan Berg of the Brookings Institution nevertheless provides a telling illustration of how many snags there may be in implementing programmes of fortification based on these materials. One of the most obvious difficulties is the frequently large difference of cost between naturally grown cereals of the kind which are grown in developing countries and the manufactured foodstuffs intended to replace them. Thus the hopes for the manufactured foodstuff called Incaparina, an ingenious blend of materials derived from soya beans and oil seeds, have been in part frustrated by the cost, which turns out often to be as much as four times the cost of the flour which it is meant to replace in Latin America.

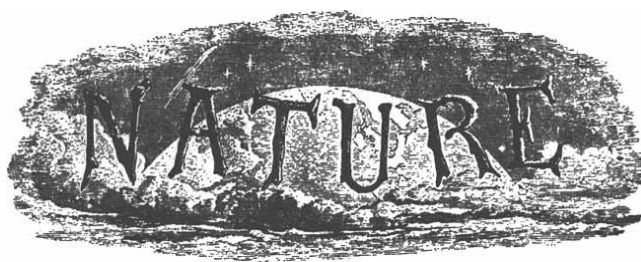
Making sure that the protein supplements are consumed by those who need them most, usually the poorest sections of a community, is another formidable obstacle to this easiest of technical solutions. Indeed, Mr Berg points out that in circumstances in which a population may already be accustomed to spend more than 60 per cent of its personal income on food, as in the larger cities of the developing world, an invitation to buy new protein supplements may have the effect of diverting spending power from other foods necessary to keep body and soul together. From this, of course, it follows that the mere provision of protein supplements is not sufficient, and that developing countries in which protein malnutrition is endemic probably have no way of meeting the social need which confronts them except by developing the kinds of child care services which can ensure that suitable foods are available at the critical times in the course of development, weaning particularly. And this, of course, is the point at which the aid-giving nations should concentrate their attention. If such programmes are to be effective, it is clear that they will have to deal not merely with the provision of protein supplements but with the health care of children in the round. This is merely another illustration of what seems by now to be a general principle—in aid programmes of all kinds, it is uncommonly hard to solve definable problems in isolation.

This is why there is much to be said for an attempt to work out more permanent devices for the amelioration of protein deficiency. Fish protein concentrates and even the products of the chemical industry may have an important role in the years ahead, but with the welfare programmes needed to make full use of them, they are only stop-gap solutions. In the long run, it will be more valuable if ways can be found of increasing the indigenous supply of protein in developing countries. As luck will

have it, at least two important lines of development have recently been opened up. First, plant breeding has made clear that it is possible to increase the yield of essential amino-acids in wheat and other cereals. There is especial interest in strains of wheat now being developed in the United States which contain larger proportions of lysine than more primitive varieties. Further ahead, of course, is the promise of what will happen when the plant breeders turn their attention to the leguminous plants, peas and beans in particular, which already provide large proportions of protein.

There is also great promise in deliberate attempts to improve the availability of animal protein in developing countries, although it will probably be an uneconomical use of resources to aim at setting up in the developing world facilities for breeding, killing and eating cattle comparable in sophistication with those which have made Texas beef a cardinal virtue in North America. But there are also limits to what the oceans will eventually provide—even if the potential yield of pelagic fisheries is much greater than is at present supposed, it is improbable that fisheries will ever yield much more than 150 million tons of fish a year, roughly twice the present harvest of the seas. In the circumstances, there is much to be said for the exploitation of methods of farming fish in fresh-water ponds, for it has already been demonstrated that in suitable circumstances the yield of protein from fish-ponds can be the most economical method of turning solar energy into essential nutrients. This is why the aid-giving agencies which are now—not before time—turning their resources to the problems of malnutrition should spare some of their energy for the long-term solutions.

100 Years Ago



Aurora Island

NATURE for May 25 (which has only just reached this part of the world) contains a note respecting the reported disappearance of Aurora Island in the New Hebrides. In that note the small upraised coral island of that name north-east of Tahiti is confounded with Aurora—a high volcanic island—more than 40° to the west of the former. It is scarcely to be wondered at that the mistake should be made when the name of the island is alone given; but when "Aurora Island, one of the New Hebrides group," is spoken of as being to the "north-eastward" of the well-known island of Tahiti one feels surprised at the misconception.

Has it yet been clearly defined to which Aurora the report refers, and is it not more probable that the captain's chronometer was out, or that his reckoning was incorrect, than that either island has really been submerged? A few months ago Dr. George Bennett, F.L.S., of Sydney, New South Wales, showed me a sketch which he made of Aurora in the New Hebrides some years ago. From that the island appears very mountainous, and the map of Melanesia, in Petermann's *Geographische Mittheilungen* (1870), makes it about twenty miles long and 2,000ft. high.

S. J. WHITMEE

Samoa, South Pacific, Nov. 4, 1871

From *Nature*, 5, 365, March 7, 1872.

OLD WORLD

Bringing Back the Lunar Bacon

from our Soviet Correspondent

LUNA 20 has arrived back from the Moon with samples of rock from the lunar mountains. Although these samples can weigh only a few grams—compared with the many pounds of lunar material returned to Earth by the Apollo programme—they may be of crucial significance to astronomers concerned with the age and origin of the Moon. Indeed, many planetary scientists would willingly trade the bulk of the Apollo Moon samples, which seem to be chiefly young material, for a small amount of rock from the mountains, where it is believed that the rocks are the oldest on the Moon—some 4.5×10^9 years old, according to current theories.

The snag has been, from the American point of view, that it is simply too dangerous to attempt to land a manned spacecraft in the lunar mountains. The fate of Luna 18, which apparently failed to carry out a similar task to that now successfully accomplished by Luna 20, highlights this; of all the tasks which the Russians could have chosen, this mission perhaps most clearly shows the advantages of unmanned exploration. This is not to say that manned projects are to be avoided—there is room for both manned and unmanned missions in the scientific exploration of space. It would, however, be foolhardy to suggest that NASA has any prospect of obtaining rocks from the lunar mountains, just as it would be foolhardy to suggest that the Russians have any hope of landing men on the Moon in the near future.

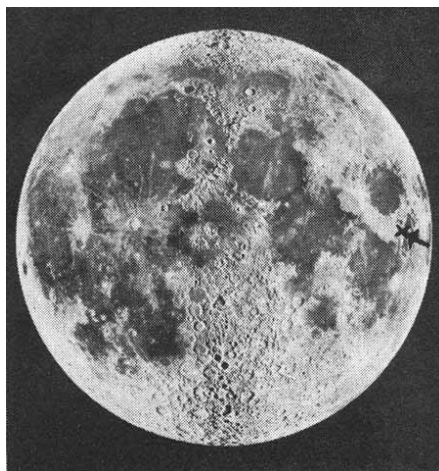
Luna 20 is the latest in a series of Russian missions which have proved strikingly successful. Luna 16 returned the first automatically gathered samples of Moon rock in September 1970; Luna 17 carried the first Lunokhod, which operated for many months in the Sea of Rains; Luna 18 failed to carry out the mission which Luna 20 has now accomplished; and Luna 19 has been orbiting the Moon since September 1971, apparently taking photographs and studying gravitational and magnetic anomalies, possibly so that Luna 20 might succeed where Luna 18 failed.

The landing site of Luna 20 was some 120 km north of the region from which Luna 16 recovered specimens (see figure). Whereas Luna 16 landed in typical mid-mare terrain, the highland area where Luna 20 touched down was

described by Soviet selenologists in *Pravda* last week as representing “the most ancient pre-geological stage of development of the Moon—the stage of condensation of lunar matter from the primary protoplanetary gas-dust cloud”. The unprecedented announcement of the failure of Luna 18 (in the past unsuccessful probes have been announced as having “completed their mission”) reflects the grave disappointment felt by the Soviet selenologists when results were not available.

Luna 20, therefore, seems almost certainly to be a second attempt at the programme planned for Luna 18. Further confirmation of the similarity of the two missions is provided from Jodrell Bank, where the touchdown of Luna 20 was monitored at 1919 GMT on February 21. The signals received were of the same general type as those from Luna 16.

Before landing, the spacecraft spent 105 hours in lunar orbit to allow fine corrections to be made to ensure a successful descent. A specimen recovery was carried out under remote control from Earth. After descent the onboard television cameras were switched on to enable the best sites to be chosen for the drilling operation. Unlike Luna 16, which used a long tube to obtain a stratified core, Luna 20, which was intended to deal with harder material, used a shock rotary annular drill. The rock samples obtained were collected, packed and sealed into containers by special manipulators. From the description



Landing site of Luna 20, close to the crater Apollonius C in the mountainous region between the Sea of Fertility (south of Apollonius) and the Sea of Crises (north of Apollonius). North is at the top of this photograph, a composite of photographs taken at first and third quarters.

issued so far of this operation, it seems unlikely that it will be possible to relate the specimens to their original depths in the ground—as was possible with Luna 16. With the specimens safe on board and using the descent stage as a launch platform in the manner of the Apollo modules, the return capsule blasted off at 2258 GMT on February 22. Re-entry was controlled by aerodynamic braking and parachutes. The descent rockets developed for the ZOND probes do not appear to have been incorporated into Luna 20. Touchdown was at 1912 GMT on February 25.

The first reported trouble arose at this stage. The capsule descended into what were described as “exceptionally unfavourable meteorological conditions”—strong winds, low cloud cover and a blinding snowstorm. An approach was made to Jodrell Bank for their latest information on the capsule. The recovery team finally located it 40 kilometres south-west of Dzhezkazgan in the Kazakh SSR, and the capsule is now on its way to the Space Research Centre of the Soviet Academy of Sciences.

PHARMACEUTICALS

Putting on a Hex

THE warning issued by Sir Keith Joseph recently on the possible dangers of using hexachlorophene has caused considerable disquiet in some medical circles. Hexachlorophene has been in use in hospitals around the world for more than twenty years, and there has been considerable disbelief that a chemical so widely used for so long can really be dangerous. Hexachlorophene is used in concentrations of about 0.2 and 0.3 per cent in many cosmetic soaps and talcum powders, and is also used medically in concentrations up to 3 per cent.

The three chief uses of hexachlorophene in hospitals are for hand washing by doctors and nurses between treatments of patients, for bathing patients with chronic skin infections (in which case it is considerably diluted), and for bathing babies in maternity units. It is these last two uses to which the warning chiefly relates.

The warning is the result of work published in both Britain and the United States, and follows a ban on the use of hexachlorophene by the Food and Drug Administration in the United States last December.

In studies undertaken by the FDA,

rats were fed high concentrations (25 mg a day per kg of body weight) of hexachlorophene for up to fourteen weeks as a result of which the white matter—but not the grey matter—of the brain was damaged. In other tests on monkeys also carried out by the FDA—full details of which have not been published—the animals were washed in a 3 per cent hexachlorophene solution for 90 days, producing a mean plasma level of $2.3 \mu\text{g ml}^{-1}$. Results have also been published in the *Lancet* (ii, 296; 1971) showing that children washed in a 3 per cent solution did absorb hexachlorophene into the bloodstream. The highest levels reached in these tests were 0.646 p.p.m.—two-thirds the concentration found to produce slight toxic effects in rats. There was, however, no evidence of any toxic effects in any of the children, and there is no evidence available of any damage to children or adults at any time when hexachlorophene has been used in accordance with the manufacturers' instructions.

The warning that Sir Keith Joseph issued was very different from the action taken by the FDA in December. The total ban that it imposed was followed by 23 hospitals in the USA reporting outbreaks of staphylococcal skin disease which hexachlorophene has been highly instrumental in reducing. As a result the FDA ruled that hexachlorophene could be used temporarily to combat an outbreak of the disease.

The attitude of part of the medical profession in this country so far has been that the warning is overcautious but everybody is playing it very safe. Boots withdrew all its products containing the chemical and the Pharmaceutical Society advised its members to warn customers of the possible dangers.

Although many hospitals have yet to decide their attitude to hexachlorophene, it seems likely that a compromise will be reached whereby regular bathing of children will be limited more than at present, but staff will continue to use the chemical for hand washing and for treatment.

Questions have been asked in Parliament this week as to what further work will be done finally to establish the safety or otherwise of the drug. Some people feel that the evidence of the drug's possible harmful effects is not convincing enough when put against the field experience with the chemical which appears to have an untarnished record.

Certainly even from the tests done so far, it would seem that permanent damage is not likely to result from use of the chemical as rats appeared to recover from the brain damage over roughly the same period of time as the chemical was administered.

ENVIRONMENT

Commoner Wades In

THE *Blueprint for Survival* came in for a virulent attack last week when Professor Barry Commoner, one of the world's leading ecologists and author of *The Closing Circle*, spoke in London at the beginning of a week long visit to Britain.

Professor Commoner arrived with both fists flying. He found himself, he said, in "severe disagreement" with the *Blueprint*.

He accused the authors of "abrogating some of the basic principles of analysis". They should not, he said, have produced a blueprint before they had analysed the problems in the way he had in *The Closing Circle*. Too much emphasis had been placed in the document on overpopulation and overproduction, rather than on the factor that Commoner holds to be all important—namely the amount of pollution each unit of production causes. It is this factor which Commoner claims has risen dramatically since 1945.

Commoner also attacked the *Blueprint* for mixing politics and science. Scientists should give people the facts and let them decide what should be done. "It is," said Commoner, "a grave mistake to tell people that a change as sweeping as the one planned in the *Blueprint* can be planned in advance by a self elected group of people." There is a real danger of elitism, he said, in the belief that you have to have a PhD to decide the answers to environmental problems. The people who should decide are the miners' union, the industrialists and housewives. As the *Blueprint* stands, he said, "it leaves itself open to a retrogressive and reactionary political interpretation".

Commoner also attacked Paul Ehrlich for criticizing his work. Ehrlich's criticisms, Commoner claims, are the result of falsifying Commoner's case and then using Commoner's own arguments to prove him wrong. At the same time Commoner also attacked Ehrlich for placing too much emphasis on population as the chief cause of the environmental crisis. At most, Commoner said, the growth in population is only responsible for one fifth of the growth in pollution. Ehrlich's criticisms of his book, said Commoner, "are simply dead wrong".

Professor Commoner also said that he was not as pessimistic as Ehrlich about the green revolution. Techniques such as microbial nitrogen fixation were making it possible to grow high yield wheat strains in the laboratory without the use of fertilizer; further, he argued that the increasing shortage of minerals in the world could be met by saving copper, zinc and other metals in the same way we now save gold and silver.

But while Professor Commoner explored the mingling of science with politics he made it quite plain that as far as he is concerned there are certain characteristics of the private enterprise system that are incompatible with ecological principles; what he wanted to see was an "economic democracy".

SCIENCE POLICY

Accountability to Whom?

THE chairman of the Agricultural Research Council, the Hon. J. J. Astor, claimed last week that implementing Lord Rothschild's proposals for the ARC would make the work of the council less accountable. At present parliamentary questions can be directed to one ministry only—the Department of Education and Science—but if more than three quarters of the ARC's budget is transferred to various government departments it would not be clear to whom questions should be addressed.

Mr Astor and other members of the Agricultural Research Council were giving evidence before the Select Committee on Science and Technology on their reactions to the reports of Lord Rothschild and Sir Frederick Dainton. Sir Frederick's report was initiated by the suggestion made at the end of 1970—following an enquiry whose results were never published—that the ARC be transferred to the Ministry of Agriculture, Fisheries and Food. Mr Astor pointed out that one of the principal effects of the insecurity has been that the ARC has failed to appoint a permanent secretary to succeed Sir Gordon Cox who retired last year. The job is now filled in a temporary capacity by Sir Ronald Baskett, who has come out of retirement, and although several people had been approached to take on the position no one is willing to take the risk until the future is clearer.

The views of the ARC were very similar to those expressed the previous week by the Medical Research Council, although the ARC did not fall into the same political traps. Dr K. L. Blaxter, director of the nutritional research institute at Rowett near Aberdeen, considered that MAFF is not "uniquely qualified to judge the country's needs" because the ARC also carries out research into health and problems of the environment—topics in which MAFF has no expertise. The ARC, according to Dr Blaxter, "can do the job properly".

Professor M. Ingram, director of the Meat Research Institute, was concerned that if MAFF was put in charge of the research now carried out by the ARC it would not provide sufficient support for long term research. He cited his own experience when he was employed by the Ministry of Agriculture.

At that time—ten years ago—Professor Ingram said the ministry was only interested in quick answers to questions and it was not at all interested in financing long term “speculative experiments”. For this reason he left the ministry to find a better atmosphere for research.

Professor Ingram also dismissed the myth that “the ministry knows”. When a member of Lord Rothschild’s staff came to see him last year while Rothschild’s report was being prepared he was asked whether the priorities within his institute agreed with those laid down by MAFF. Professor Ingram admitted then that he was unaware of any priorities imposed by the ministry and that he had been unable since then to find out what the priorities were—if indeed any existed.

Dr H. C. Pereira, director of East Mallory Research Station, was concerned that the transfer of responsibility to the ministry would lead to the cutting off of funds for long term research projects, leading to job insecurity. In these circumstances there would probably have to be staff redundancies and it would be difficult to persuade scientists to work at the institutes. Also, Dr Pereira thought that it would be difficult to persuade scientists to become directors of institutes, and that they would also be reluctant to sit on councils.

UNIVERSITIES

An Upper Limit

THE number of students in British universities in 1980 could be 420,000 according to the University Grants Committee annual report published last week (HMSO, £0.24). The UGC based its estimates on a survey of building sites which universities can rent or buy within the next eight years. Of the 420,000 students envisaged, only 200,000 or 47.5 per cent could be resident within universities if all options on sites are taken up. The student population in 1970 was 228,189 with 87,000 or 38 per cent of these accommodated in halls of residence.

The UGC also reports that if options are taken up on sites that have been zoned for university expansion, but on which no contracts, agreements to purchase, or compulsory purchase orders exist at present then 500,000 students could be admitted to universities in 1980 with 230,000 accommodated within halls of residence.

This estimate of the possible student population is not a commitment to provide finance for this number by 1980, according to a spokesman for the UGC. He also said that it was highly unlikely that there would, in fact, be that many university students in eight years’ time. In 1963 Lord Robbins said

that a total student population of more than 500,000 should be aimed for by 1980 with 350,000 of them in universities and the remainder in other institutions of higher education. The Education Planning Paper of June 1970 said that there should be 394,000 students in universities in England and Wales by 1981, but there has been no ministerial support for this plan.

The UGC has succeeded in making some inroads into the problems of student housing during the past year. During the previous five years residential places within universities increased at the rate of 4,000 a year, but following a survey last year the UGC decided to press ahead and encourage the universities to expand at the rate of 10,000 places of accommodation a year until 1977. During the present academic year universities have set into motion plans that will result in the completion of more than 8,000 resi-

dential places during 1972–73, a total which the UGC considers “a fair start”. The finance for new building does not come entirely from the government, and the universities have obtained loans totalling £8 million—more than half of which was obtained from building societies. The subsidy from the UGC will amount to £3 million to £4 million a year for four years.

The report also shows that the staff/student ratio has remained substantially unchanged since 1960–61. In that year the ratio was 7.93 whereas in 1969–70 it was 8.16. During this time, however, the yearly expenditure for every full-time student has increased from £794.27 to £912.52 at 1967–68 prices. The cost of departmental salaries in the decade has only increased from £352 to £374 a student, and most of the increase has come from a near doubling of the cost of “academic services” and a 125 per cent increase in local government rates.

UNIVERSITY SALARIES

More Than Increases

As was to be expected, university teachers have been awarded increases in salary which raise their total salary bill by about 7.5 per cent to about £120 million a year. Although this is only about half that claimed by the Association of University Teachers (AUT) on behalf of most academic staff in universities, it forms only part of quite a comprehensive agreement.

The new salary scales, which are backdated to October last year, are shown in the table. In the past, only a maximum has been laid down for the salaries of senior lecturers and readers, but under the new agreement a national scale will come into force and those at present in these grades will either receive an increase of 7.5 per cent or move onto the bottom of the scale, whichever is most beneficial to them. Two further steps are to be added to the top of the lecturer scale over the next two years so that the maximum salary for lecturers will become £3,852 in October this year and £3,999 in October 1973, at which stage there will be sixteen steps in the scale.

There are also two clauses in the agreement which improve the lot of those taking up lecturing posts in their

middle or late twenties. Lecturers appointed at ages of 26 or more will in future be placed on at least the third step of the scale, and the present efficiency bar at the eighth point of the scale will now operate five years after the end of a compulsory probationary period of three years, or, exceptionally, four. A spokesman for the AUT said this week that this is in line with its policy of raising standards.

The AUT has also succeeded in having the discretionary payments suggested by the Prices and Incomes Board in 1969 abolished. The aim was to encourage good teachers, as opposed to good researchers, by making merit awards worth one per cent of the non-professorial salary bill. The money saved by the ending of this scheme—one fiercely opposed by many academics—was redistributed during the course of the negotiations.

Prospects of promotion to senior lecturer are also enhanced by an increase in the maximum allowed proportion of senior lecturers and above from 35 per cent to 40 per cent. The AUT says, however, that the figure is at present about 31 per cent because of shortage of money within universities, and that although it hopes that the proportion will be raised to the new ceiling, it may be that it will turn out to be lower than 40 per cent.

Salary Scales for University Teachers

	New scale	Old scale
Lecturers	£1,641 to £3,705	£1,491 to £3,417
Senior lecturers and readers	£3,852 to £4,734	Up to £4,401
Professors	Minimum £4,850	Minimum £4,533
	Average £6,003	Average £5,610
London allowance	£162	£100

EDUCATION

Appeal to the LEAs

THE Architectural Association's School of Architecture is now "facing the future with confidence" according to Professor Alvin Boyarsky, chairman of the School.

After the doubts about the school's future since the breakdown of its merger talks with Imperial College, University of London, in 1970, the school claims to have overcome its immediate financial problems. Strict budgeting and a £120 a year rise in the school's fees last year have combined to give the school enough money for the next three years—even allowing for a 9 per cent annual rate of inflation—without the need for any increase in income. The school's £37,000 overdraft has been paid off, and by 1976, when its lease in Bedford Square expires, about £500,000 will be available to acquire new premises. This money is the result of the appeal fund launched several years ago to pay for a projected new building in South Kensington and of the unexpected sale of the AA's playing fields.

The school has now submitted evidence of its financial viability to local education authorities (LEAs) in the hope that they will support the British students which the school wants to admit this autumn.

The school's dilemma is that the very independence which gives it its particular character makes it ineligible for a direct grant—as it would be if it were part of a university or polytechnic. As

a result its fees of £580 are much higher than the £100 or so that an LEA grants to students at other architectural colleges. The AA points out that this is misleading because after taking direct grants to other schools into account, sending a student to the AA's school saves the country about £200 a year. With 300 students at the school in any one year whose fees are paid by local education authorities, this according to the AA represents an annual saving of £60,000.

The local education authorities, naturally enough, see it differently. To them, sending four students to the AA school can cost them as much in fees as sending twenty students elsewhere, and not surprisingly they have asked the AA to find ways of reducing its fees.

What the AA would like, although it is careful not to be specific, is to have its cake and eat it. A grant from central government would solve its financial problems, but the AA is not prepared to give up its independence by joining a university or polytechnic to qualify. It is therefore up to the LEAs—unless the government is prepared to allow for special cases in areas other than pay disputes—to foot the bill.

If the AA's new submission is rejected, the school intends to carry on by expanding the number of overseas students and taking only those British students who can afford to pay, or for whom grants of some sort can be found. It would be ironic, however, if the LEAs refused to support the school just when it has begun to put its own house in order.

POLLUTION

Waste Not, Want Not

"A WELL trained staff and a high degree of informed citizen participation are the ultimate keys to [the planning and operation of] a successful solid wastes programme" according to a World Health Organization report (*Solid Wastes Disposal and Control*, WHO, Geneva, 1971). The report, written by an international team of multidisciplinary scientists and public health officials, also recommends that governments should be helped in their planning of solid wastes programmes by "international, bilateral and private agencies". These agencies would provide finance as well as professional expertise.

The report, by recommending international participation in solid wastes programmes, flies in the face of the present practice of leaving general management of such programmes either to local government or to industry. The report also recommends that every country should have, at ministerial level, a body of experts to collect and collate data on solid wastes management and to draw up codes of practice for the guidance and training of personnel involved in wastes disposal. Governments should also set up regional authorities to "optimize the use of available land and to minimize haulage costs".

The committee emphasizes that international action is also needed to ensure that "adequate weight is given to public health considerations in all environmental policy making of broad scope and significance". The recent international agreement to limit dumping in the North Atlantic (see *Nature*, 235, 414; 1972) is only a small part of the overall plan envisaged by the committee, and it would like to see international agencies identifying specific wastes and disposal practices that are potentially deleterious to health and should therefore be subject to international control. Monitoring systems should also be run on an international basis as should any dumping of waste in outer space—this method of getting rid of radioactive waste was a suggestion canvassed recently by the chairman of the US Atomic Energy Authority.

Research and development is needed to develop methods and equipment for waste disposal—in particular in the underdeveloped countries. Such research, the committee feels, is again an international problem because inefficient waste disposal threatens the health of more than the inhabitants of that particular country. Industrial experience of disposing of toxic wastes would be helpful in applying waste disposal techniques on a world wide scale.

ECONOMY

Magic One Per Cent

BRITAIN is planning to increase the amount spent on overseas aid during the next five years. The planned expenditure until 1975–76 (*Public Expenditure to 1975–76*, HMSO, £0.68) shows that Britain will increase aid from the £206 million that is being spent this year to an estimated £290 million in 1975–76. Not only is this an absolute increase at an average rate of 7.6 per cent a year but as a proportion of the total public expenditure of the government the sum allotted increases from 0.86 per cent to 1.08 per cent. Details of the increases are shown in the table where all prices are 1971–72 prices with no allowance made for inflation.

Overseas aid covers British assistance to developing countries through

international organizations and the chief recipient of aid is the International Development Association, but the United Nations Development Programme and other UN agencies receive some contributions.

Even at the estimated aid for 1975, contributions from the government to the underdeveloped countries will still be far short of the one per cent of Britain's gross national product that the government, at the request of the United Nations Conference on Trade and Development (UNCTAD), undertook to provide by 1975 (the GNP for the 1971 calendar year was £42,877 million). Private funds, however, are expected to add to the official government sum and the government has said that the total aid from government and private sources is "expected to make a substantial contribution to the UNCTAD 1 per cent target . . . by 1975."

Public Expenditure on Overseas Aid (£ Million) as a Percentage of Total Public Expenditure

1970–71 (provisional)	1971–72 (estimate)	1972–73 (estimate)	1973–74 (estimate)	1974–75 (estimate)	1975–76 (estimate)
206.0	215.8	234.5	245.2	266	290
0.86%	0.88%	0.93%	0.95%	1.02%	1.08%

NEW WORLD

NSF's Bid for Relevance

by our Washington Correspondent

OFFICIALS of the National Science Foundation last week made their first pitch to Congress in this year's negotiations over the Foundation's budget. They were given an easy ride by the few members of Mr John Davis's subcommittee on research and development who were present to hear Dr H Guyford Stever, NSF's new director, and senior members of his staff outline the programmes for which they are seeking appropriations of \$653 million in fiscal year 1973 (which roughly spans the 1972-73 academic year).

Although Mr Davis opened the proceedings with the warning that he is not happy that the Foundation is again seeking to reduce its support of graduate education, the committee had few harsh words to say about the NSF's growing stake in applied research activities, and seemed to welcome the new programme by which the National Science Foundation and the National Bureau of Standards hope to test methods for encouraging non-federal investment in research and development. Last year the committee, which sets upper limits for the money that Congress can appropriate (the actual amount of money to be made available is decided by the appropriations committees), lopped some \$30 million off the Foundation's budget request for applied research and put the money back into its science education and institutional support programmes. The ploy was, however, frustrated by the Office of Management and Budget which withheld some of the Foundation's education support grants, thereby making NSF that much poorer.

Undeterred, NSF officials are again asking Congress to sanction increases in funding for mission oriented research, and decreases in graduate and institutional support grants. Relevance is the watchword and, in line with the administration's overall strategies for research and development (see *Nature*, 235, 188; 1972), the NSF is seeking to involve itself in projects which are likely to provide tangible benefits by contributing to the solution of pressing social problems or to economic growth. Officials of the Foundation take pains to point out, however, that support of basic research is not being allowed to suffer from emphasis on applied research.

Last week's budget hearings (they are also being held this week) provided

NSF officials with their first public opportunity to explain the thinking that lies behind the proposed new experimental R & D incentives programme, and to outline their proposals for the programme of Research Applied to National Needs (RANN)—a collection of projects which last year bore the brunt of Mr Davis's committee's axe. The Foundation is asking for appropriations of \$22 million for the incentives programme, \$2.5 million for another new programme aimed at understanding better how the innovation process works in the civilian sector, and \$80 million for RANN. Together these programmes add up to about 15 per cent of the appropriations requested for the Foundation.

Outlining the research and development incentives programme, Dr Raymond Bisplinghoff, deputy director of the Foundation, said its chief aim is to increase non-federal investment in research and development by a variety of incentives. Because the process by which investments in research and development lead to marketable products is not well known, especially outside defence and space industries, he said that the project will work on an experimental basis by trying out a number of methods of overcoming possible blockages to investment and to the transfer of technology from one sector to another.

The project will be roughly divided into three parts, the first of which will be aimed at stimulating cooperative research undertakings between, for example, universities and industrial firms, non-profitmaking organizations and research associations. Another section of the project is designed to stimulate investment in research and development in the service sector, which traditionally lags behind other sectors of the economy in productivity, and which accounts for some 64 per cent of the work force, and the third arm of the project will be geared towards making the best use of human resources in technological innovation, for example, by encouraging temporary exchange of personnel between industries and between industry, government and the universities.

As for the initiatives designed to promote cooperation on research projects, the NSF's chief weapon would be a matching grant. The idea is that industry would be encouraged to sponsor research at universities, and its outlay would be matched by NSF grants to the university. Alternatively, Bispling-

hoff told the committee that the NSF may seek to close the gap between industry and the universities by sponsoring scientists from industry to work on NSF sponsored research projects in universities. Another possible approach is to stimulate investment in fundamental research through industrial associations, research associations or professional societies.

The experimental incentives programme will be managed and planned by a network of advisory committees and a programme office reporting directly to Dr Bisplinghoff. A key element of the management plan will be an advisory board composed of representatives from industry, the universities, state and local governments, labour unions and industrial associations. Proposals for experiments to be funded by the programme will be evaluated by NSF staff working with the advisory board, and final screening and review will come from a coordinating committee composed of officials of the National Science Foundation and of the Department of Commerce, which will also be conducting its own technology initiatives programme, geared more towards the marketing end of the innovation process.

Explaining the need for such an incentives programme, Bisplinghoff told the committee that "there is ample evidence of a direct and positive correlation between the nation's support of R & D, its general economic growth, productivity increases, and the creation of new products and services". But "the central problem we face is one of developing recognition and capability by industry of the full spectrum of opportunity for the exploitation of R & D throughout the civilian economy in meeting societal needs".

The Foundation's second large stake in stimulating research which may have important applications in solving social problems or which may lead to economic expansion is the RANN programme, described last week by Dr Alfred J. Eggers, NSF's new assistant director for research applications. In the past, RANN has been viewed by academic scientists and by some members of Congress with mixed feelings. For one thing, many have suggested that the National Science Foundation, traditionally the bastion of support for basic research, lacks the capability for managing applied research. (Until 1968, when the Act under which the Foundation operates was changed, it was legally constrained to confine its

activities to support of basic research and science education.) Others have been sceptical about the ability of science and technology to provide solutions in the short term to complex social problems and another frequently heard criticism was that the Foundation has used the trendiness of the RANN programme as a means of swinging extra funds from Congress.

But there are signs that the Foundation has taken steps over the past year to come to grips with many of these criticisms. New guidance for RANN is coming from an inter-agency committee under the chairmanship of Edward E. David jun., the President's science adviser, and NSF officials cite the fact that many eminent scientists are now supported by the RANN programme as evidence of its scientific respectability. Moreover, the programme stands a better chance of emerging more or less unscathed from the appropriations process on Capitol Hill because there has been a shift in emphasis compared with the Foundation's budget request last year, with research on energy production, regional environmental systems and municipal systems and services chief objects of much of the new concentration of effort.

Dr Eggers explained to the committee last week that the thrusts of the RANN programme have received a searching review by the National Science Board, advisory committees of the Foundation and the new RANN coordinating committee. In deciding whether a specific project should be supported, factors such as its importance to national needs, whether science and technology can have "a unique and substantial impact on the problem", and whether it is ripe for a focused research effort, are taken into account. The RANN coordinating committee, which is composed of representatives from six other federal departments and agencies, also decides whether the NSF is the best agency for the job.

The upshot of this review is that energy research carries off the bulk of the funding designed for advanced technology applications (the RANN programme is divided into five sections—advanced technology applications, environmental systems and resources, social systems and human resources, exploratory research and problem assessment, and the intergovernmental science programme), and projects on earthquake engineering and fire research are also set for an injection of funds. The energy research programme includes some long lead-time projects, such as research into solar power utilization on a large scale, together with studies aimed at defining energy needs, while the earthquake engineering programme will include design studies of an earthquake simulator approximately 100 feet square.

OUTER PLANETS

From Jupiter to Saturn

by our Washington Correspondent

THE National Aeronautics and Space Administration last week formally announced that it intends to launch two Mariner class spacecraft in 1977 to fly by Jupiter and then Saturn. These missions will replace the grand tour of the outer planets, scrapped by NASA for budgetary reasons, which would have taken spacecraft close to all the outermost planets during the 1970s and 1980s.

Announcing NASA's plans for the Jupiter/Saturn mission during budget hearings held by the House Committee on Science and Astronautics, Dr John Naugle, associate administrator for space science, pointed out that although the mission is still not completely defined, it is expected to cost about \$360 million compared with the estimated cost of \$900 million for the full blown grand tour. Since NASA is under orders to keep its budget at about the \$3,000 million level for the next few years, funds for the grand tour were cut out of the agency's 1973 budget request and the Mariner flyby of Jupiter and Saturn is perhaps the most ambitious outer planetary mission that planetary scientists could hope for.

Launched by a Titan/Centaur rocket, the spacecraft should fly by Jupiter about 18 months after setting off and, accelerated and deflected by Jupiter's gravitational field, it will reach Saturn two years later. Although the mission's objectives might be altered by data relayed back from Jupiter by Pioneers F and G, they will almost certainly include taking a close look at satellites of both planets and at the enigmatic rings of Saturn. Of special interest is Titan, a satellite of Saturn which is about the same size as Mercury and which is the only planetary satellite in the solar system known to have an atmosphere. There is also a possibility that the trajectory of the second spacecraft will be altered in mid-course to take account of data radioed back from Saturn by the first.

Like the Pioneer spacecraft, the proposed Mariner flybys will derive their power from radioisotope thermoelectric generators because they will fly too far from the Sun to use solar power and because the length of the mission precludes the use of any other type of battery. The spacecraft will each be able to carry more than 100 pounds of scientific instruments, including television cameras—the Pioneer spacecraft has the capacity for only 65 pounds of instruments.

A statement put out by NASA last week points out that the decision to opt for Mariner class flybys of Jupiter and

Saturn does not preclude sending Pioneer spacecraft to orbit Jupiter and Saturn in the late 1970s. The Space Science Board of the National Academy of Sciences has, in two successive reports last year, emphasized the need for maintaining a solid research programme on Jupiter and to a lesser extent Saturn, whatever decisions are taken about the grand tour, but there is some doubt about the risk of orbiting Jupiter. The problem is the largely unknown danger to scientific instruments from the large radiation bands around the planet, but the hazards may be better known when results from Pioneer F are analysed.

The announcement of the Mariner flybys last week has been greeted with general approval by planetary scientists, although the approval has been tinged with disappointment at the scrapping of the grand tour. Dr Naugle said, for example, that the proposal has been "warmly endorsed" by the Space Science Board as a "strong and flexible programme which is a reasonable next step in planetary exploration". The Space Science Board had advised NASA early last year that the original concept of the grand tour should not be undertaken unless the total space science budget were increased considerably. NASA nevertheless went ahead and asked for \$30 million to proceed with designs of a thermoelectric outer-planetary spacecraft (TOPS) in its budget request for 1972. But Congress cut the request to \$20 million and instructed the agency to take another look at its plans for outer planetary space-flight, whereupon a second panel of the Space Science Board was convened and reported in November last year (see *Nature*, 234, 246; 1971). This second panel warmly endorsed the grand tour concept, but suggested that if insufficient funds are available it should not be allowed to crowd out intensive studies of Jupiter and Saturn.

Dr Francis S. Johnson of the University of Texas, who was chairman of the second Space Science Board panel, said last week that although he is disappointed that NASA's budget could not accommodate the grand tour, the Mariner class flybys of Jupiter and Saturn should help to answer some of the more important questions about those two planets. But Dr Carl Sagan, of Cornell University, said that he is "very disappointed" about the decision to scrap the grand tour. He pointed out that there is a good argument for taking a quick look at the outermost planets because of the possibility of finding something completely unexpected. He added that the self-repairing and testing computer that was to have been developed for the TOPS spacecraft would have had great potential value for application in different fields.

NEWS AND VIEWS

Astrophysical Abundances Under Fire

ON page 15 of this issue, G. Worrall and A. M. Wilson deliver the latest in a series of critical commentaries on the validity of abundances of elements in stellar atmospheres deduced from the study of absorption lines. The basic criticism hinges on the simplifying assumption (or rather approximation) of local thermodynamic equilibrium, which is usually introduced in such work although it certainly never holds rigorously and is known to lead to substantial errors in the case of the very hottest stars. (In this context a "substantial" error may be defined as one exceeding a factor of 2 in the abundance ratio of the element relative to hydrogen, for hydrogen usually provides the continuous background against which absorption lines are seen; errors much smaller than this are achievable in a limited number of cases only, because of various uncertainties that would persist even if local thermodynamic equilibrium were strictly valid.)

The question is, then, whether there is convincing theoretical or observational evidence that the assumptions made in such abundance analyses are reasonably good or very bad. According to Worrall and Wilson it can be shown that they are very bad for the following reason. Imagine what happens to the equivalent width (that is, integrated intensity) of an absorption line as the relative abundance or oscillator strength of the atoms producing it is increased indefinitely from zero, leaving other characteristics of the stellar atmosphere unchanged (this relationship is called a curve of growth). At first the equivalent width increases linearly with the product of abundance and oscillator strength; then it flattens off as a result of saturation at a level governed by the Doppler width of the line due to random motions in the line of sight; and finally it increases again (usually in proportion to the square root of the abundance) when its strength has become so great that substantial damping wings develop.

The skeleton in the cupboard is the fact that the observed flat portion of stellar curves of growth is usually too high to be accounted for (within the framework of the usual assumptions) by thermal Doppler broadening alone, and therefore a purely empirical additional Gaussian broadening parameter, known as "microturbulence", is introduced. There is no independent evidence for any such effect of the required order of magnitude in most stars, and in the case of the Sun—the only star that can be studied in sufficient detail to hope to obtain such evidence—there is evidence against it. Worrall and Wilson quote cases of analyses in which abundances are acknowledged to be quite uncertain because they involve lines on the flat part of the curve of growth that are more sensitive to the microturbulence assumed than to the abundance itself; but their more important conclusion seems to be that all spectroscopic abundances are to be treated with grave suspicion because of the invalidity of the basic theory.

This is by no means the first time that this problem has been raised. In connexion with the problems of solar

microturbulence, it is of interest to note that, as knowledge of oscillator strengths has improved, the figure quoted for solar microturbulence has tended to decrease. Furthermore, the figure can be eliminated altogether by using the van der Held curve of growth which refers to absorption with no remission in a cold, uniform gas, and the same result could undoubtedly be derived for a stratified model of the photosphere by neglecting re-emission in the lines. In many giants and supergiants, however, even this treatment would lead to a flat part of the curve of growth that is too high to be accounted for by thermal Doppler broadening alone, and in this case additional broadening of the absorption coefficient must be postulated because there is simply no other way of getting the result. Furthermore, the existence of chromospheres and mass motions is evidence for hydrodynamic motions, some of which may very plausibly be on a sufficiently small scale to broaden the line absorption coefficient; because the observations are usually not sufficient to provide more than one parameter, the Gaussian approximation seems to be a not unreasonable device. Thus although it is perfectly true that abundances derived from lines on the flat portion of the curve of growth have large errors, the arguments of Worrall and Wilson do not prove that the theory is so bad that one cannot use lines on the linear and square-root branches.

Fortunately the calculations can be taken further, and various tests can be made for the case of the Sun and quite a number of stars which show that the approximations in the theory are adequately good for the purpose. To begin with, it can be shown theoretically that local thermodynamic equilibrium gives an excellent approximation to the visible continuum in all but supergiants and the very hottest stars. Theoretical investigations of the spectrum of sodium, and of the very weak forbidden absorption lines of O I and Fe II, in the solar spectrum suggest that only minor departures from local thermodynamic equilibrium occur in equivalent widths, and the structure of the photosphere is certainly adequately known from measurements in the continuum.

Now within the factor of 2 mentioned earlier, the solar abundances of carbon, oxygen, sulphur, calcium, iron and nickel deduced from forbidden and permitted lines are all in agreement, so that it is hard to see how any errors due to departure from thermodynamic equilibrium could exceed this factor. (A few years ago, there was a much larger discrepancy for iron, both with respect to forbidden absorption lines and with respect to emission lines in the corona, but certainly the bulk of this has been removed by new laboratory measurements of permitted-line oscillator strengths.) As far as other stars are concerned, many uncertainties due to oscillator strengths and other factors can be reduced by working differentially and again the same sort of consistency can be obtained in stars that can be readily compared with the Sun, for example, members of the Hyades cluster. The case of a metallic-line A star, quoted by Worrall and Wilson, in which the

differential abundance change increases systematically with atomic mass, may be perfectly real—why not?

Thus the considerations given by Worrall and Wilson are a salutary reminder of how much cross-checking is needed before accepting spectroscopic evidence of abundances; they do not prove that the whole exercise is fallacious.—B.E.J.P.

Targets for Penicillin

ONE of the essential properties of a clinically useful antibiotic is selective toxicity; that is, its mode of action must be such that it kills or inhibits the growth of a pathogenic organism but is not dangerously toxic to the cells of the animal host. By 1957 it had been established that penicillin was a specific and selective inhibitor of the biosynthesis of bacterial cell walls and that it intervened in a sequence of reactions which does not occur in animal cells.

Further progress came from a study of the structure of bacterial cell walls and of their biosynthesis. The bacterial cell is bounded by a fragile cytoplasmic membrane which controls its osmotic equilibrium. This is surrounded by, or interwoven with, a more rigid cell wall which can be regarded as partly composed of a single macromolecule of enormous size, built up from a limited number of constituents and known variously as mucopeptide, peptidoglycan or murein. The backbone of this polymer is made up of chains of an aminopolysaccharide composed of alternate residues of N-acetylglucosamine and N-acetylmuramic acid, an amino sugar which apparently does not occur in animal tissues. The residues of N-acetylmuramic acid are linked to small peptides and the latter are cross-linked to one another by means of an inter-peptide bridge. Penicillin irreversibly inhibits the transpeptidation reaction by which the cross-link is formed, and which is the last step in the synthesis of the cell wall murein. This inhibition may partly be attributable to a resemblance in conformation of penicillin and the D-alanyl-D-alanine fragment at the end of the peptide chain of the cell wall precursor.

In last week's *Nature* (235, 426; 1972) Hartmann, Hölte and Schwarz suggest that there is a second target for the action of penicillin in *Escherichia coli*. They present evidence that penicillin blocks the activity of two murein hydrolases which may well be key enzymes in cell wall biosynthesis. Murein hydrolases, or wall autolysins, can be visualized as a means of providing acceptor sites in the murein polymer to which newly synthesized disaccharide-peptide units can be transferred.

Hartmann and his colleagues have developed a sensitive test system for the detection of murein hydrolase activity. After disintegration of *E. coli* cells, hydrolase activity was detected in both the particulate and soluble fractions. The active particulate fraction yielded two enzymes, one of which was inhibited by penicillin whereas the other was not. The first was characterized as an endopeptidase. Of two hydrolases present in the soluble fraction, one was inhibited by penicillin and shown to be a glycosidase.

It is suggested that the endopeptidase described here may be identical with the transpeptidase from a particulate fraction of *E. coli* which has been described by Izaki *et al.* (*J. Biol. Chem.*, 243, 3180; 1968). The concentra-

tion of penicillin required to inhibit the transpeptidation reaction by 50 per cent was found by Izaki *et al.* to be three units per millilitre, which is similar to the five units of penicillin per millilitre required for 50 per cent inhibition of the endopeptidase activity in the test system of Hartmann *et al.* A considerably higher concentration of penicillin, 400 units per millilitre, was, however, required for 50 per cent inhibition of the glycosidase activity.

Schwarz, Asmus and Frank (*J. Mol. Biol.*, 41, 419; 1969) reported that penicillin has two distinct morphological effects on *E. coli*. At ten to fifty units per millilitre cell division is inhibited whereas cell elongation is blocked only at concentrations higher than 100 units per millilitre. Strominger has recently suggested (*Proc. Roy. Soc. Lond.*, B, 179, 369; 1971) that there may be separate transpeptidases involved in septation and elongation of bacterial cells. Hartmann *et al.* now suggest that the endopeptidase is involved primarily in cell division and the glycosidase in cell elongation, and that both enzymes are targets for the physiological action of penicillin on *E. coli*. They further note that the observation that the overall rate of murein synthesis in *E. coli* is reduced in the presence of penicillin (H. J. Rogers, *Bact. Rev.*, 34, 194; 1970) can be explained by the inhibition of glycosidase activity, because it might be expected that this would reduce the number of starting groups available for polysaccharide chain synthesis.

It is interesting to recall that Collins and Richmond (*Nature*, 195, 142; 1962) suggested that the action of penicillin might be explained in part by its structural resemblance to N-acetylmuramic acid, and hence that the antibiotic may block the action of an enzyme which handles a derivative of the amino sugar during murein synthesis. But the question whether the glycosidase is concerned with the lethal action of penicillin remains to be answered.—From a Correspondent.

How Many Globin Genes?

THE differentiation of animal cells usually results in the synthesis of large amounts of a small number of proteins or even a single protein. Myoblasts differentiating into muscle, for example, synthesize contractile proteins, erythroblasts synthesize haemoglobin, plasma cells synthesize immunoglobulins and so on. But how is the differential expression of the genome of a differentiating cell achieved? Are the genes which specify particular proteins amplified by some as yet unknown mechanism or do all cells have many copies of all genes or can the synthesis of a vast amount of one or a few species of proteins be achieved simply by enhancing the rate and extent of transcription of just one or two copies of the relevant genes?

At first sight it may seem rather unlikely that cells should amplify particular genes during differentiation but it has been shown beyond reasonable doubt that during the maturation of eggs in at least some species of insects and amphibia the number of copies of ribosomal RNA genes in the maturing oocyte is increased, and the ribosomal RNA genes are amplified. But to what extent can generalizations be drawn from these findings? In a recent issue of *Nature New Biology* (235, 231; 1972), Bishop, Pemberton and Baglioni describe some nucleic acid hybridization experiments in which they

have attempted to measure the number of copies of globin genes in duck reticulocytes and from which they conclude that there are probably no more than five copies of the globin genes per cell.

Bishop *et al.*'s experiments have the following rationale. The rate at which a constant amount of duck globin messenger RNA will hybridize to a vast excess of denatured duck reticulocyte DNA at any particular temperature will depend on the number of copies of the globin genes in that DNA. The greater the number of gene copies present, the faster the globin messenger RNA molecules will hybridize to those genes. If the rate at which a small amount of unique RNA will hybridize to a vast excess of DNA containing just one copy of the corresponding gene is known, it can be used to calibrate the rate of hybridization of globin messenger to reticulocyte DNA and allow the number of copies of globin genes in the reticulocyte DNA to be estimated.

But, as anybody who does little more than glance at what Bishop and his colleagues have to say will immediately realize, there are formidable practical and theoretical obstacles to carrying out such hybridization experiments. For one thing, measuring the rate of hybridization of a unique RNA to DNA with one copy of the corresponding gene in practice boils down to measuring the rate of hybridization of RNA transcribed *in vitro* off *Escherichia coli* DNA with an excess of *E. coli* DNA and then an estimated correction factor has to be applied to compensate for the differences in complexity of duck and *E. coli* genomes. Furthermore, completely pure globin messenger RNA preparations are not available; 10S RNA from duck reticulocytes undoubtedly contains globin messenger molecules but it may well contain other RNA species. And for reasons which are obscure and may be manifold, in practice considerably less than half the globin messenger RNA hybridizes to large excesses of reticulocyte DNA.

In spite of the uncertainties which factors such as these engender, however, the results which Bishop *et al.* report suggest, but certainly do not prove, that each reticulocyte genome contains at most ten and probably only five or fewer copies of the globin genes. If this conclusion is correct gene amplification cannot play an important part in the differentiation of red blood cells but other groups have recently reported hybridization experiments which on the face of things indicate that in reticulocytes of mice and chicks there may be tens of thousands of copies of the globin genes. Bishop and his colleagues give reasons for not taking these experiments at their face value but how the groups concerned will react to the criticisms remains to be seen.

PHOSPHOLIPIDS

More about Less

from our Molecular Biology Correspondent

AN awestruck recipient once summed up Macauley's table-talk with the verdict, "Sir, his information is greater than society requires". This, I imagine, is also how most readers would now view the continuing ooze of data that results from putting phospholipids in this state and that into various expensive machines. Not to allow fatigue and prejudice to get the upper hand, however, one should all the same continue to sift the new data for the occasional hard fact that may turn out to have a bearing on the nature of real membranes.

It is faintly surprising that the resources in particular of spin labelling and nuclear magnetic resonance (NMR) in regard to such systems are not yet exhausted, even if the point of diminishing returns has by and large been reached. Haque *et al.* (*J. Biol. Chem.*, **247**, 157; 1972) have looked at the proton magnetic resonance (PMR) spectra of lecithin in chloroform solution, and have observed generous shifts of the signals from the protons of the quaternary amino group methyls and of the bound water, when the concentration or temperature is changed. These evidently reflect the formation of micelles, and regardless of the factors that go to determine the shifts, their concentration and temperature profiles offer a very satisfactory, and apparently precise method of defining the association equilibrium. Haque *et al.* extract the micelle number, which is only about three at all temperatures, the association constant, and the related thermodynamic parameters.

Lee *et al.* (*Biochim. Biophys. Acta*, **255**, 43; 1972) have examined this same system, among others, in terms of spin-lattice relaxation times, measured by the trendy new technique of Fourier transform NMR, whereby radio-frequency pulses are used to irradiate the sample, and the individual decay processes that are contained in the resulting signal are resolved by Fourier analysis. A decrease in mobility due to self-association is again noted. The spin-lattice relaxation times are characteristic of the state of the lecithin, the inverted micelles in chloroform—polar head-groups pointing inwards—showing increased mobility towards the non-polar end of the chain, and contrariwise in aqueous systems. Vesicles in water show, clearly reflected in the NMR spectrum, the phase transition provoked by a change in temperature (at 43° C in the case of dipalmitoyl lecithin). Although the vesicle remains unchanged in size, large increases in line width occur when the temperature falls below this point, indicating a co-

operative freezing of segmental motion. The introduction of cholesterol brings about changes in relaxation time and line width, in a manner suggesting that the motion of the lecithin chains is inhibited, especially near the hydrophobic tail.

The effect of cholesterol, as manifested in the proton magnetic resonance spectra, is also the preoccupation of Darke *et al.* (*J. Mol. Biol.*, **63**, 265; 1972). Elsewhere the same group (Finer *et al.*, *Biochim. Biophys. Acta*, **260**, 49; 1972) confirm that sonication of the spherulitic particles that are formed when egg lecithin is dispersed in water turns them into closed spheres bounded by a single bilayer. This emerges from a measurement of the number of head groups perturbed when the paramagnetic manganous ion is added to the sonicated solution. In broad agreement with the work of other groups, Finer *et al.* find that the proportion of head groups so affected corresponds well enough to the calculated fraction occupying the outside surface of the hollow sphere. The PMR spectra of such bodies are sharp (Finer *et al.*, *ibid.*, 59), as is by now well known, and in order to analyse the factors governing the line widths in these systems, Finer *et al.* have examined the spectra at a number of frequencies from 60 to 300 MHz. There is in fact a dependence of width of the hydrocarbon proton resonances on frequency, which, it is conjectured, arises from anisotropic modes of motion rather than adventitious effects, such as field inhomogeneity. The narrow lines are consistent with the relatively small size of the sonicated vesicles, which tumble sufficiently rapidly to give rise to averaged dipolar interactions—a condition which does not obtain in the larger particles present in unsonicated dispersions. The conclusion is that it is legitimate to interpret changes of line widths in the spectra of the vesicles in terms only of differences in segmental motion of the hydrocarbon chains—a conclusion which had generally been taken for granted.

To revert then to the effect of cholesterol, Darke *et al.* find in the first place that a sufficient concentration of the steroid in the lecithin particles completely represses the transition to the liquid-like state that normally occurs on raising the temperature. From the relative effects on the various lecithin proton resonances it can also be inferred that only a part of the molecule makes contact with the cholesterol. Whereas the hydroxylic region of the lecithin displays sharpening and thus increased mobility, that of the quaternary amino methyls is broadened. Because it is thought that the hydroxyl group of the cholesterol protrudes into

the head-group layer, it is not unreasonable to posit, as Darke *et al.* do, a hydrogen bonded interaction between the two species at this point. The 1:1 stoichiometry fits the observation that no more than an equimolar amount of cholesterol can be incorporated into the particles. When the proportion of cholesterol is appreciably less than this, the PMR spectra give evidence that it exists in two states, complexed and free. From this it would seem to follow that the phases are present in the bilayers, one of which consists of clustered cholesterol molecules. If, as has been suggested, such clusters exist also in real membranes, the gross transport characteristics must be considered in terms of the properties of both phases.

The application of phosphorus NMR to phospholipid systems was to be anticipated, and has been duly reported by Barker *et al.* (*Biochim. Biophys. Acta*, **260**, 161; 1972). Differences between the spectra of dispersions of different phospholipid species are seen, as also is a thermal transition of the spin-spin relaxation time. This therefore evidently gives another measure of the head-group mobility.

PALAEOICHTHYOLOGY

Gogo Placoderms

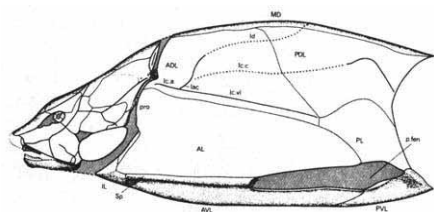
from a Correspondent

IN 1963, H. A. Toombs, of the British Museum (Natural History), visited the Western Australian Museum, Perth, and saw there some limestone nodules of Upper Devonian (Frasnian) age from Gogo Station, a cattle farm in the Fitzroy Trough, Western Australia. Toombs saw that these nodules contained some exceptionally well preserved fish and made a short collecting trip which was followed by a much larger joint expedition in 1967 by the British Museum (Natural History), the Hunterian Museum (University of Glasgow) and the Western Australian Museum.

The importance of these fish lies in their preservation in calcareous concretions from which uncrushed skeletons can be extracted with dilute acetic acid. These skeletons are so well preserved that they have been mistaken for Recent material by the uninitiated. The expedition collected approximately two tons of fossiliferous material including about a thousand fish of Upper Devonian age and some 2,300 phyllocarid crustaceans. The fauna is rich in both species and individuals, and research on it is being undertaken by R. S. Miles (placoderms and dipnoans), S. M. Andrews (rhynchonellans and dipnoans) and B. G. Gardiner (actinopterygians). This fish fauna is probably the most important of its type and age so far discovered.

R. S. Miles (*Phil. Trans. Roy. Soc., B*, **263**, 101; 1971), in the first major publication on the fauna, gives a thorough description of the skeleton of one of the placoderms, *Holonema*. This genus has been known from scattered fragments for more than 100 years and, although world-wide in distribution, it has until now been very imperfectly understood. Miles's descriptions, including concise details of the upper jaw apparatus, show for the first time what *Holonema* really looked like. Furthermore, Miles convincingly demonstrates that the holonematids belonged to the more dominant group of arthrodires, the brachythoracids and not to the dolichothoracids (arctolepids) as Obruchev (1964) and Romer (1966) assumed. Palaeontologists now have this major arthrodire group (Brachythoraci) known from primitive forms such as *Coccosteus* (Miles and Westoll, 1968), advanced types like *Dunkleosteus* (Heintz, 1932) and divergently specialized members such as *Homosteus* (Heintz, 1934) and *Holonema*. The new evidence, together with that on internal structure in other placoderms by Stensiö (1963), has enabled Miles to discuss the vexed questions of jaw suspension and snout structure in placoderms. Miles shows that the placoderms had a suspensory hyomandibula, albeit with unique relations to the hyomandibular nerve, and were not aphethochoydean; but his evidence on the snout rather undermines previous evidence which related placoderms to elasmobranchs. Because this was the most important piece of evidence for relating placoderms to elasmobranchs a reappraisal of the relationship could be a valuable study.

The Gogo fauna is a mixture of Northern Hemisphere and indigenous species. Actinopterygians are represented by members of the Stegostrachelidae, crossopterygians by *Onychodus*, dipnoans by *Griphognathus*, *Chirodipterus* and *Holodipterus* and the placoderms, in addition to *Holonema*, include *Coccosteus*, *Eastmanosteus*, *Bothriolepis*, *Ctenurella* and "*Ptyctodus*". The fauna, when fully described, will increase understanding of Devonian zoogeography, but only when considered with the known positions and connexions between the continents, obtained from geophysical



Miles's restoration of *Holonema westolli* sp. nov. (from *Phil. Trans. Roy. Soc., B*, **263**, 154; 1971).

studies. By the time geophysicists can tell palaeontologists more of seas and the connexions of the continents during the Devonian, the Gogo fauna should be completely described and then the question of zoogeography can be properly tackled. Miles presents the last part of his review of the Holonematidae as a first step in unravelling the zoogeography but then wisely leaves the subject for a later article.

VOLCANISM

Etna's 1971 Eruption

from a Correspondent

THE 1971 eruption of Etna, Europe's largest and most active volcano, was one of the biggest for many years, lasting from April until June. It attracted the attention of volcanologists from many countries, notably Britain, France and Italy, and a meeting in London on February 9 and 10 was arranged under the aegis of the Royal Society to bring together the many individuals concerned from these three countries to obtain a coordinated view of the eruption and to discuss ways of advancing research on the volcano.

It was manifest from the meeting that the eruption had served three very useful functions. First, it demonstrated very clearly that there is an urgent need for geophysical monitoring equipment on the volcano, which compares very favourably for ease of access and frequency of activity with the volcanoes of Hawaii which have been comprehensively instrumented. Second, it stimulated a number of workers to go into the field and make quantitative observations on the eruption, covering a range of phenomena from the viscosity of the lavas to the composition of the gas phases present and to the development of magnetic fabrics within the cooling lavas. In particular, rapid X-ray fluorescence techniques made it possible for relatively large numbers of samples of the lava to be analysed, more than for any previous eruption of Etna. Third, it emphasized, as Professor A. Rittmann (International Institute of Volcanology, Catania) pointed out, just how little is known of the overall tectonic situation of Etna, and its relations to geophysical concepts.

One of the most stimulating areas of discussion at the meeting was whether any kind of magma differentiation process had operated during the eruption and what kind of magma reservoir existed beneath the volcano. Drs R. Romano and C. Sturiale (International Institute of Volcanology, Catania) presented analyses showing a slight but systematic variation in composition of lavas erupted during the eruption, with the lavas formed latest being rather more silicic than the earliest. They

interpreted this variation as the result of pneumatolytic and gravitative differentiation taking place in the lava column, with denser, ferromagnesian minerals being subtracted from the magma during the later stages of the eruption. Dr J. C. Tanguy (Laboratoire de Géomagnétisme du Parc St Maur) challenged this view, however, and presented further analyses showing very little variation; he accepted, though, that his analyses may not have been representative of the very earliest and last lavas.

In spite of the lack of geophysical evidence, it was agreed that there is no large "magma chamber" underneath the volcano, and it was accepted that some differentiation could have taken place in dyke-like lava columns. Professor Rittmann, stressing this point, pointed out that the ancestral Etnean volcanoes had formed by progressive migration of volcanic activity westwards across a set of NE-SW trending faults and fractures, and suggested that Etna was fundamentally similar to the Icelandic type of volcanism, with magma rising up dykes and fissures in response to dilational tectonic stresses.

New light was also thrown on the viscosity of moving lava flows and its significance. Dr G. P. L. Walker (Imperial College, London), talking in general terms, discussed the factors which influence the lengths reached by individual flows, and suggested that the most obvious factor, viscosity, was probably less important than the rate of effusion of the lava. He emphasized the scarcity of even these very basic data, and urged the need for more systematic work in the future. There could well be direct practical implications from such work, because if measurements could be made on the rate of flow and viscosity of a lava at its source, it might well be possible to predict how far it will travel and, therefore, whether it presents a serious hazard to towns and villages situated downslope. Dr F. Gauthier (Université d'Orsay) gave Dr Walker some encouragement and described detailed observations he had made on the rheology of the Etna lavas. He stressed that the viscosity was not only a factor of the temperature of a lava but also of its bubble and crystal content and said that laboratory studies of the effect of these factors on artificial glass melts were currently in hand.

The meeting was a great success, and will undoubtedly be a significant step towards promoting concentrated, co-ordinated research in Etna in the future. It was good to learn, in the closing minutes of the meeting, that a start had already been made on the geophysical side and a team from Imperial College is undertaking geodetic surveys of the upper part of the volcano.

FRESHWATER FISH

Too Many Mouths

from a Correspondent

Few freshwater fishes have been studied as intensively as the brown trout. Aspects of its biology have absorbed workers now for many years and because of its sporting, and thus commercial value, are likely to do so on an increasing scale in the future. A recent article by M. Kennedy and P. Fitzmaurice on growth and food of trout in Irish waters (*Proc. Roy. Irish Acad.*, 71 (B) 18, 269; 1971) is a welcome contribution to knowledge of the biology of this fish.

Freshwater fishes in Ireland are accepted as of considerable value as a sporting attraction, and under the aegis of the Irish Inland Fisheries Trust their exploitation has been supported by a research programme into the biology of the common fishes and management of fisheries. Kennedy and Fitzmaurice's article is therefore to be seen as not just a valuable contribution to the biology of the trout, but as a product of an enlightened national programme for research into the management of a valuable resource.

Previous authors have drawn attention to the disparity in size and growth between trout from alkaline and acid waters, and Kennedy and Fitzmaurice confirm this relationship. They suggest

that trout in alkaline waters grow well because such waters are more productive of food. Acid waters are unsuitable for certain molluscs (an important food for trout); the acidity tends to delay the breakdown of organic matter and the recycling of nutrients; moreover, their coloured water inhibits growth of submergent vegetation in deeper areas. These are certainly factors in the poor growth and small size of trout in acid waters. Treatment of acid loughs with limestone and inorganic fertilizers results in some improvement in growth, but Kennedy and Fitzmaurice consider that such adjustments of pH are not economically justifiable. Their solution for improving growth rates in acid lakes is a reduction in suitable spawning sites (by preventing access to the tributary streams), for the problem is basically one of too many mouths for the available food.

The food of Irish brown trout is varied and within each water they are opportunist feeders, taking whatever is most abundant seasonally or locally of a suitable size. An interesting note on the food of the large "ferox" trout, the predatory trout of the biggest Irish loughs, suggests that they owe their size at least in part to the general poverty of the invertebrate fauna which forces them to take to fish-eating at an earlier age than is usual in trout.

Trout fisherman will be advised to

Isolation of Concanavalin A Receptors

In the past two years lectins—glycoproteins extracted from various plant seeds—have come into the limelight chiefly because they agglutinate cancer cells and cells transformed by tumour viruses much more readily than they agglutinate corresponding normal cells. It seems that the transformation of a cell to malignancy causes considerable changes in the structure and/or composition of the cell surface and lectins provide a convenient way of detecting these changes.

One lectin in particular, concanavalin A, may even provide a method for assaying malignancy. As Inbar, Ben-Bassat and Sachs reported in *Nature New Biology* last week, there seems to be a positive correlation between a cell's increased susceptibility to agglutination by concanavalin A and its increased malignancy when inoculated into a susceptible host animal. There is, by contrast, according to Inbar *et al.* no such correlation between malignancy and susceptibility to agglutination by two other lectins, wheat germ agglutinin and soybean agglutinin.

If this correlation can be independently confirmed, the isolation and characterization of the receptor molecules in cell membranes which bind

concanavalin A will become a matter of considerable importance and in next Wednesday's *Nature New Biology* (March 8) Allan, Auger and Crumpton report a technique for doing just that. They have made columns of 'Sepharose 4B' to which they covalently attached concanavalin A molecules. After washing the columns with appropriate sugar solutions to remove unbound concanavalin A they have used them to fractionate by affinity chromatography detergent solutions of the plasma membranes of pig lymphocytes. Their idea was simply that if the concanavalin A receptor molecules survive exposure to detergent they should bind to the columns while other membrane components should pass through the columns, and that is what happened.

A set of five glycoproteins can be eluted from the columns with solutions of the sugar methyl- α -D-glucopyranoside which is known to dissociate complexes of concanavalin A and its cell receptor molecules. And, as expected, these eluted glycoproteins competitively inhibit the metabolic activation of lymphocytes by concanavalin A. Concanavalin A receptor molecules have therefore been at least partially purified by these means.

temper their fishing with a knowledge of surface geology, for it is the limestone loughs which hold the fastest growing and largest trout in Ireland.

TUMOUR VIRUSES

Activating Virogenes

from our Cell Biology Correspondent

THE hypothesis that the genomes of the normal cells of vertebrates contain genetic information required to specify RNA tumour viruses has, since it was first mooted by Bentvelzen (1968) and Payne and Chubb (1968) and then Huebner and Todaro in their eponymous oncogenes and virogenes article, dominated the thinking of many if not all tumour virologists. The idea is deceptively simple; if all animal cells vertically inherit oncogenes, the transformation of any particular cell to malignancy depends on whether its oncogenes are switched on. Likewise, the liberation of an RNA tumour virus from the cell depends on whether its virogenes are also expressed.

This hypothesis can, of course, account for the transformation of any and every cell by any and every carcinogen and the fact that most cancer cells do not seem to release an RNA tumour virus is simply explained away by saying such cells have active oncogenes but inactive virogenes. Indeed the chief problem with the hypothesis has always been that it is seemingly impossible to test, but that has not prevented quite compelling evidence in its favour being collected.

During the past five years, for example, it has been shown quite unequivocally that normal chick cells may specify an antigen indistinguishable from the group specific antigen of the avian tumour viruses and such gs^+ chick cells also contain a helper factor which complements and allows to replicate defective Bryan high titre Rous sarcoma virus, RSV(O). Last year Vogt and Friis found that several gs^+ chick cells spontaneously release a virus called RAV.O, which by a variety of biophysical and biochemical criteria can be classified with the avian leukosis viruses. It seemed therefore that gs^+ cells do indeed inherit the potential to specify and release an avian leukosis type virus as predicted by the oncogene hypothesis. But what about gs^- cells which do not carry the gs antigenicity: do they also have the genetic potential to specify a leukosis virus? Weiss, Friis, Katz and Vogt (*Virology*, **46**, 920; 1971) have now shown that they do. Using a variety of chemical carcinogens and mutagens and ionizing radiations Weiss and his colleagues have induced both gs^+ and gs^- cells to start to release a virus which very closely resembles, and may be identical to, the

spontaneously released virus RAV.O. The virus can be induced not only from cells of domestic chicks but also from the red jungle fowl *Gallus gallus*.

The induced virus contains reverse transcriptase, a single stranded 70S RNA genome and virion polypeptides similar to those of the avian sarcoma leukosis viruses. The induced virus can also act as helper for the replication of the defective Bryan high titre Rous sarcoma virus and in the taxonomic sense at least it must be classified with the avian leukosis viruses. Whether it can actually cause leukosis in chicks remains to be established; if it cannot cause leukosis or transform cells in culture the possibility of rendering this virus oncogenic by, for example, repeatedly passaging it through chick cells transformed to malignancy by chemical carcinogens will have to be investigated.

What is true of chicks should, of course, be true of other vertebrates if the oncogene hypothesis is correct, and Rowe *et al.* (*ibid.*, **46**, 866; 1971) have now shown that apparently virus free cells of clones of AKR mouse embryo cells, on exposure to physical carcinogens, or, significantly, on transformation by SV40, are induced to liberate a murine leukaemia virus identical to that which can cause leukaemia in AKR mice. The obvious conclusion seems to be, therefore, that both chicks and mice do indeed inherit the genetic potential to specify an RNA virus of the C-type sarcoma leukaemia virus type, and that expression of this potential can be induced by carcinogenic agents, albeit at a low frequency. Those tumour virologists wedded to the oncogene hypothesis now have powerful ammunition with which to assail the sceptics.

CANCER RESEARCH

Oncogenic Viruses

from a Correspondent

A SINGLE cause for all cancers has always been an attractive postulate, though heavily criticized by clinicians who see patients with many and apparently different malignant diseases. Those researchers who work with chemical carcinogens have tended to think that their favourite compounds, for example, polycyclic hydrocarbons or nitrosamines, are the most likely candidates for the chief environmental cause of cancer. Virologists have during the past decade begun to think that their pets are the most significant aetiological factor. At the British Museum (Natural History) on February 14, the sixth meeting in the series on the principles of clinical and experimental oncology gave some hint that the virologists have a point.

Dr P. M. Biggs (Houghton Poultry

Research Station) said he wished to make it clear that there seemed to be nothing special about oncogenic DNA viruses in either shape, size, encapsulation, molecular weight of nucleic acid or base ratios. They can be found among most of the recognized classes of viruses. There is the clear suggestion in such a statement that there may prove to be far more viruses which can have oncogenic effects than have so far been detected—there is even the possibility that all viruses can be oncogenic under appropriate circumstances. Aside from the taxonomic categorization, three types of virus can be distinguished; those which have been shown to cause tumours in experimental animals, for example, polyoma and SV40; those which lead to benign tumours naturally, for example, certain pox and papilloma viruses; and those which lead to malignancies in nature, for example, Marek's disease virus in poultry.

Inferential evidence suggests that one viral genetic coding unit only is required to bring about the transformation of a cell to a malignant precursor cell. This in itself provides some validation for the notion of the oncogene. Dr Biggs pointed out that in many instances the virus was involved in a non-productive infection in rapidly growing tumour cells but that this could not be taken as indicative of lack of the viral genome. In Marek's disease, for example, a lymphoproliferative neoplasia, it is extremely difficult to identify the causative virus anywhere except in the feather follicle epithelium. In practice, vacuum cleaned debris from infected birds has been shown to contain many virus particles.

Professor W. F. H. Jarrett (University of Glasgow) spoke of the oncornaviruses particularly in fowls, mice and cats, in which they can lead to leukaemia or sarcoma. All these viruses, independent of their species of origin, have an identical physical structure and method of replication. The manner in which they succeed in instructing their host cells to synthesize replicas by production of an RNA-DNA polymerase is well known, at least in principle. Again the evidence shows that the cells in which malignant transformation occurs are often not those in which virus is produced. Professor Jarrett indicated that the strongest evidence against the extreme form of the ubiquitous oncogene theory, which requires vertical transmission from generation to generation of genetic information, perhaps in the form of an RNA viral genome or its DNA replica, is that horizontal transmission can be made to occur and it does lead to malignancy. In these circumstances Occam's razor excises the oncogene.

Can Astrophysical Abundances be Taken Seriously?

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The determination of the abundances of elements rests on several assumptions, particularly the existence of micro-turbulence, for which there is no experimental or theoretical justification.

ONE of the classical problems of astrophysics is to determine the relative abundance of elements in the atmosphere of a star from observations of its line spectrum. In the 1920s Saha, and Fowler and Milne showed, through their work on ionization equilibrium, that the gross differences in appearance of stellar spectra were due to variations in temperature and that although some stars have chiefly hydrogen lines in their visible spectrum, whereas for others the hydrogen lines are weak (and the lines of metals, like iron, very strong), it was not to be inferred that the relative abundance of heavy elements in the atmospheres of the latter is necessarily greater than in the former. The basic concepts underlying abundance analysis have not changed since that time although, of course, as more has been learned about atomic absorption processes, and as better data on the relevant atomic parameters have become available, they have been used within the existing framework.

Much has been learned about the principal variations in the abundance of heavy elements relative to hydrogen. Generally speaking, the older stars have a smaller proportion of heavy elements, consistent with the view that such elements are synthesized by nuclear fusion in stars and subsequently at least partially returned to the material from which successive generations of stars will form. The correlations which have been found between heavy element abundance and kinematics of the stars can be interpreted through a fairly simple picture of galactic evolution¹. As more has been discovered about stellar evolution through computation of improved stellar models, and as more details of nucleosynthetic processes have been unravelled, interest has grown in the detailed variations in abundance of individual elements in a particular star and in variations from star to star. Those stars for which the line spectrum is obviously "peculiar" have received much attention. Recently it has been claimed² that there exist old giant stars with significantly greater abundances of heavy elements than

young stars in the solar neighbourhood. These were called super-metal rich and it is suggested that they are not uncommon. If true, this result is of great importance for our understanding of galactic evolution, but everything depends on the reliance to be placed on the abundances obtained. A substantial minority of people working in spectroscopic analysis and radiative transfer feel that the methods of analysis can allow but little confidence in the results. In textbook treatments, the fundamentals of the analysis of stellar spectra are obscured by technical detail and the published criticism of the methods of analysis is diffused through many conference reports, so we shall try in this article to describe the basis on which abundance analysis is carried out and present our criticisms of it.

Basis of Stellar Spectroscopic Analysis

The essential feature underlying abundance analysis is the assumption that local thermodynamic equilibrium prevails in a stellar atmosphere, that is that all relevant distribution functions, except that for the photons themselves, are thermal and determined by the local temperature T . The atoms are distributed among ionization states according to the Saha equation and have a Boltzmann distribution among excitation states, so that a determination of the number in any particular state suffices to determine the abundance of the element. The radiative emission coefficient ϵ_ν , and the absorption coefficient κ_ν , which together determine the radiation field throughout the atmosphere, are related by the Kirchhoff-Planck relation $\epsilon_\nu = \kappa_\nu B_\nu(T)$, where $B_\nu(T)$ is the Planck function. The way in which line spectra are interpreted can be illustrated very easily if one simplification, which changes none of the principles involved, is made. This is that the temperature varies with depth in the atmosphere in such a way that the Planck function varies linearly with optical depth. (The optical depth increment, in an increment of depth dz , is $\kappa_\nu dz$.) Then it can be shown that the flux of radiation received from a star at frequency ν is equal to the Planck function at that depth in the atmosphere at which the total optical depth, for radiation at that frequency, is $2/3$. The relation between the absorption coefficient and the absorption line in the stellar spectrum is shown in Fig. 1. In Fig. 1a the absorption coefficient is plotted as a function of wavelength shift $\Delta\lambda$ from line centre. (The dashed lines should be ignored temporarily). Its form is determined by the absorption coefficient for an average atom, a Lorentz profile determined primarily by pressure effects, convoluted with the thermal velocity distribution function:

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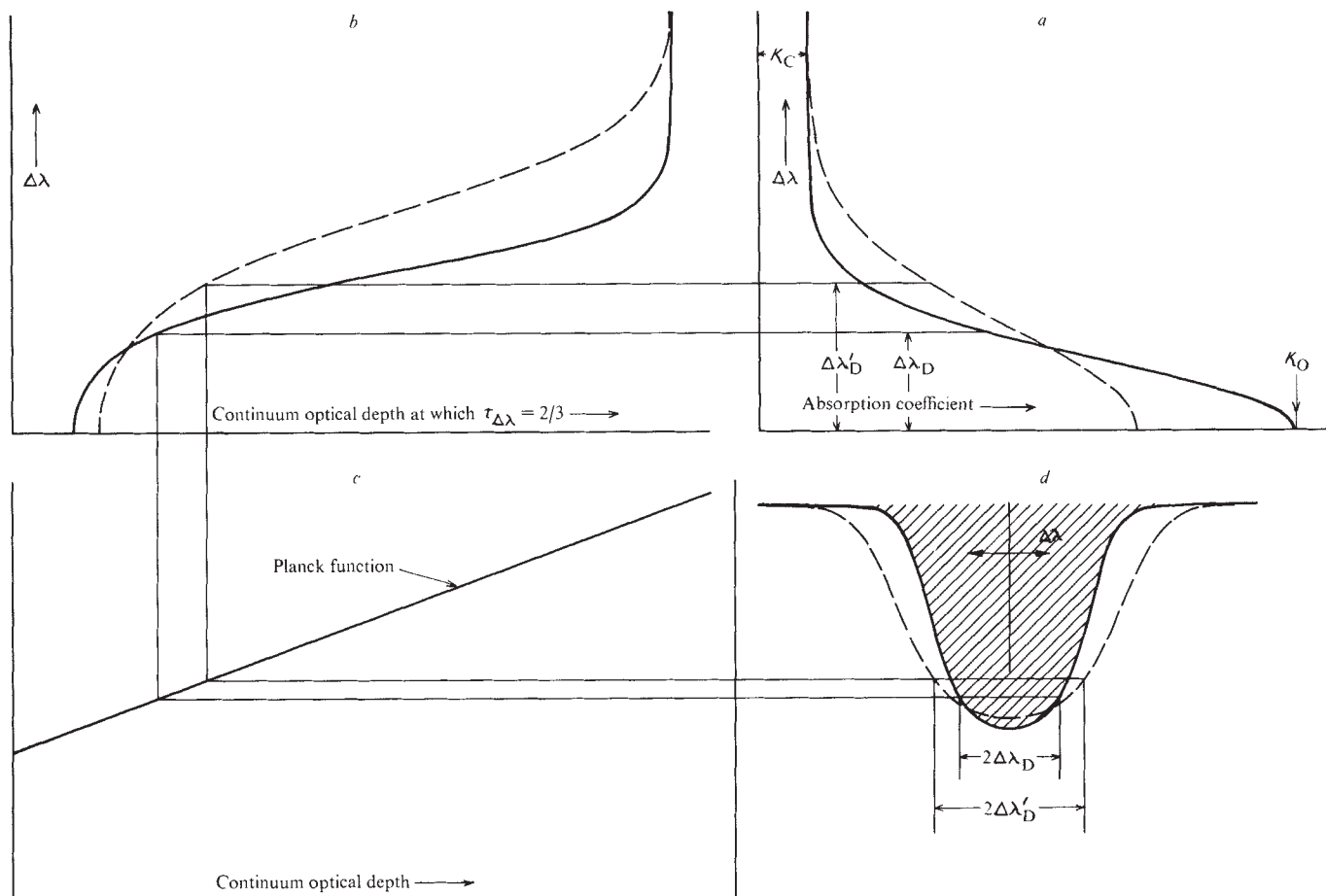


Fig. 1 The relation between the absorption coefficient of the atmospheric material and absorption line in the stellar spectrum, according to the concepts underlying spectroscopic analysis. *a*, The absorption coefficient as a function of wavelength shift $\Delta\lambda$ from line centre; κ_0 is the absorption coefficient at line centre, κ_c that for continuum radiation. ---, An increase of 50% in the Doppler width, $\Delta\lambda_D$. *b*, The corresponding variation, with $\Delta\lambda$, of the continuum optical depth at which the total optical depth is $2/3$. *c*, The Planck function, at the central wavelength of the spectral line, as a function of continuum optical depth. *d*, The line profile in the stellar spectrum. For simplicity it is assumed that the absorption coefficient does not vary with depth in the atmosphere and that the Planck function varies linearly with continuum optical depth.

the Doppler width, which is the wavelength shift corresponding to the most probable atomic speed, is indicated by $\Delta\lambda_D$. The absolute value of the absorption coefficient, which can be specified by its value at line centre, κ_0 , is determined by the number density of the particular type of atom in the relevant state of excitation. At large wavelength shifts the absorption coefficient tends to the continuum value κ_c ; the aim of abundance analysis is to determine the ratio κ_0/κ_c .

Corresponding to this absorption coefficient, the continuum optical depth at which the total optical depth is $2/3$ is shown, as a function of $\Delta\lambda$, in Fig. 1*b*. From this and the Planck function which varies linearly with optical depth as in Fig. 1*c*, the absorption line in the stellar spectrum turns out to be as shown in Fig. 1*d*. The variation of the Planck function with wavelength can be neglected over the wavelengths involved. We assume that the absorption coefficient does not vary with depth in the atmosphere and although this is inconsistent with a variation of temperature with depth it is adequate for this illustration. The relation between temperature and optical depth, which is not necessarily such as to lead to a linear variation of the Planck function, is usually obtained in one of two ways. Either an atmospheric model is computed, assuming hydrostatic, radiative and local thermodynamic equilibrium, for the appropriate effective temperature and gravitational acceleration or, if the effective temperature is not very different from that of the Sun, the solar temperature/depth relation is used (but scaled to the different stellar temperature).

Abundance analyses are not based on the line profiles, which are very difficult to obtain, but on the total absorption ascribable to the line (called the equivalent width, and shown shaded in Fig. 1*d*). In principle this quantity can be determined with equipment not capable of yielding the line profile—for instance by narrow-band photometry—but its determination depends on the location of the continuum. This is a simple matter in the ideal situation treated in Fig. 1, but in many spectra, especially of the cooler stars, the lines are so close together that the position of the continuum is by no means obvious. In fact the equivalent width is found to depend on the dispersion³: “. . . we observed a remarkable difference between equivalent widths of the same line obtained on spectra of different dispersions. . . . The fact that the equivalent widths are smaller on high-dispersion spectra, even though taken with the same spectrograph, is well known and has been observed by many authors”.

Results of Abundance Analysis

This physical basis does not, however, provide a self-consistent interpretation of the observations. In fact the abundance of an element in a particular atmosphere depends systematically on the equivalent width of the line from which it was determined. And it was pointed out by Schwarzschild in 1914 that the variation of solar absorption lines from the centre of the disk to the limb could not be understood on this

basis. Naturally in these circumstances the underlying assumptions were questioned but abundance analysis proceeded on these assumptions by the use of a device; in 1934 Struve and Elvey⁴ introduced into the analysis a quantity called microturbulence. They supposed that the Doppler width for a line was much greater than that due to thermal broadening; the additional width they attributed to non-thermal motion in the stellar atmosphere, called microturbulence because the velocity must vary on a small scale spatially. The effect of a 50 per cent increase in Doppler width is shown by the dashed lines in Fig. 1. The equivalent width of the line is increased by an amount depending on the initial strength of the line and in this way the relative equivalent widths of lines are changed. Microturbulence has been used ever since to reduce the obvious systematic errors in abundance analysis.

The adjustment thus made is usually very large, although it is only rarely that the raw results (without microturbulence) displaying the discrepancy between theory and observation are presented. A recent example is an analysis of G-type subdwarf stars⁵. For one of these, HD 140283, the deduced abundance of iron varies systematically, by a factor of 10, with the equivalent width of the line; the stronger the line the greater the inferred abundance. There is also a systematic variation with the excitation potential of the absorbing state for the line. The raw results were presented in this case because "it is almost impossible to deduce a model that will predict an entirely consistent behaviour for the deduced abundances". They suggest, however, that for this star the most probable microturbulent speed (a Gaussian distribution is always assumed) is between 2 and 3 km s⁻¹. The effective temperature is about 5,500 K so that the most probable thermal speed of iron atoms is 1.25 km s⁻¹, about half the microturbulent speed. This is typical of the relative magnitudes of microturbulent and thermal velocity deduced for dwarf stars. The microturbulent velocity is relatively greater in giant stars and even greater in the supergiants.

This quantity is not only used in the analysis for a few stars which may be thought to be in some way "peculiar" but in all analyses. It is used in a completely arbitrary manner. There are no independent observations even suggesting that such small-scale, non-thermal motion exists, much less defining its amplitude. No hydrodynamical analysis is ever given to describe the nature of the motion responsible and it is only rarely that possible effects of such motion on the structure of the atmosphere are considered. If the velocity amplitude is very large an extra term is sometimes included in the equation for hydrostatic equilibrium, but "for the lack of sound physical theory which can be handled easily by computer in the context of this problem, it is assumed that the effects of turbulence, sphericity (and breakdown of local thermodynamic equilibrium) on the temperature distribution will cancel"⁶. The obvious difficulties in interpreting microturbulence as non-thermal motion are often so great that such statements as the following are found:

"The abundances were calculated for several assumed values of V_{turb} , and that value which gave the least correlation between line strength and abundance was taken as the turbulent velocity. While the V_{turb} determined in this manner may refer to actual atmospheric motions it is formally only a parameter used to approximate any unknown or overlooked broadening by a Gaussian function" (ref. 7).

"The other free parameter that must be determined is the 'turbulence'. It should be emphasized here that this parameter need not be considered a true turbulence. It is a parameter found necessary to minimize the dependence of abundance on equivalent width and is expressed as V_t in km s⁻¹" (ref. 8). That is, an adjustment parameter has been used to make the theory agree with observation.

This use of such a parameter is surely unique in science. It is perhaps tolerated in this branch of astronomy only because it was first used so long ago, has been used continually ever since and has become deeply rooted. Many thousands of

repetitions have gone far towards making a truth. It is built into procedures of spectroscopic analysis as automatically as temperature and nowadays one is almost never confronted with the true discrepancy between theory and observation.

Even after the gross systematic errors in the results for a particular star have been removed using the adjustment parameter, peculiar systematic variations in the results for different elements and from star to star remain. Thus the results for metallic-line A stars indicate that the abundance of the elements from carbon to gadolinium increases systematically with atomic mass relative to the abundance of the same elements in normal A stars⁹. Spinrad and Taylor¹⁰ have pointed out that there are analyses which indicate a systematic variation of heavy element abundance with the effective temperature of the star. They show how unlikely it is that this effect is real. On the other hand, they argue for results obtained by approximate methods of analysis described by Deutsch¹¹. But as Deutsch states, "we must recognize that these methods produce results that are rough and not fully reliable" and "the lack of detailed information regarding atmospheric structure may limit our abundance determinations to order of magnitude estimates, even though we possess an extensive body of data". Yet it is on results obtained by these methods that Spinrad and Taylor² suggest the existence of numbers of super-metal rich stars with as much as four times the abundance of heavy elements as young stars in the solar neighbourhood. An analysis of the spectra of some of these stars by model atmosphere techniques, the basis of which we have described, indicates that the abundance of heavy elements is normal¹². The postulated microturbulent velocities are between 3 and 6.5 km s⁻¹ (these are K giant stars) and it is suggested "that some of the observable phenomena attributed to super-metal richness may result in part from an increase in the turbulent velocity parameter". Similarly, in an analysis of the silicon star HD 34452 (ref. 7), it is found that "most of the differences between our analysis and others are due to the large velocity parameter that we found necessary. By contrast with our value of 8 km s⁻¹, Casati and Hack used 2.6 km s⁻¹ and Mihalas and Henshaw used 0 km s⁻¹". They show that by changing this parameter from 8 to 4 km s⁻¹ the apparent abundance of elements is changed by as much as a factor of 5. Thus the derived abundances depend strongly on the unconstrained parameter "microturbulence".

It is often claimed that in so far as relative abundances in different stars are being discussed the results can be relied on, even though knowledge of atmospheric structure is incomplete, and the relevant atomic transition probabilities uncertain. This is a valid argument only if all other characteristics concerned in the stars involved, apart from the abundance of element X, are known to be identical. But this can never be so and indeed it is generally found that the microturbulence varies from star to star as well. This alone is evidence that "everything else" is not the same. In fact the argument is never strictly valid because the line observed in a stellar spectrum depends on the variation of temperature with depth in the atmosphere. This depends on the frequency dependence of the continuum opacity of the atmospheric material which, especially for the cooler stars, depends on the abundance of the heavy elements.

The Sun

The solar spectrum allows a rigorous test of theories of line formation in an atmosphere not merely because of the greater possible spectroscopic resolution and photometric accuracy but because the Sun displays a disk and line profiles can be observed in the radiation emitted at different directions to the local vertical in the atmosphere. For the same reason we have direct information from the continuous spectrum on the variation of temperature with depth, at least in the region relevant for the formation of the weaker lines. To achieve an approximate match with observed line profiles it is found

necessary to postulate two independent components of microturbulence—a vertical component and a horizontal component, each varying with depth. Again these are chosen without constraint, expressly to force the best possible agreement. Even so, in an analysis of oxygen lines¹³ there is “a systematic increase in the abundance from centre to limb for all permitted lines” although “the abundance differences from centre to limb or from stronger to fainter lines are all relatively small and remain within a factor 2 (except for the uncertain results of the 6157 line)”. It was found that the “Holweger model best reproduced the lines studied”. In this model both components of microturbulence decrease with height in the atmosphere, from 2.4 km s^{-1} to about 1 km s^{-1} , but the horizontal component is considerably larger than the vertical at intermediate heights, for example, 2.1 km s^{-1} compared with 1.55 km s^{-1} . Again these are the most probable speeds of an assumed Gaussian distribution.

In solar analyses it is generally assumed that microturbulence is real non-thermal motion, by contrast with what is sometimes considered in stellar analysis. In fact such analyses are sometimes undertaken with the aim of determining the solar velocity field. But it can be shown¹⁴ that even if there is a small scale velocity field in an atmosphere its effect on the line absorption coefficient can only be taken into account by microturbulence within the reversing layer concept of line formation, for which in fact it was introduced⁴. (This is a primitive concept in which it is assumed that a featureless continuum is emitted into a cool, isothermal layer in which line absorption occurs; it underlies many forms of an analytic technique, still widely used, called the curve-of-growth.) Depth-dependent microturbulence is a particularly questionable concept. Moreover, by considering the velocity field in the solar atmosphere that is inferred directly from observed shifts of spectral lines, it can be shown¹⁴ that it is very unlikely that there is any small-scale velocity field with an amplitude even approaching 1 km s^{-1} .

Local Thermodynamic Equilibrium

A fundamental weakness of all abundance analyses is clearly the blanket assumption of local thermodynamic equilibrium in stellar atmospheres. This can be valid only if collisional processes are dominant in bringing about transitions between the excitation states of an atom. It has often been shown^{15,16} that the density in a stellar atmosphere is so low that, on the contrary, radiative processes are predominant. The state of excitation in any particular element in the atmosphere therefore depends strongly on the radiation field, which, in turn, depends on the state of excitation everywhere in the atmosphere. There is a stark contest between this and the situation in the local thermodynamic equilibrium, in which the state of excitation is fixed by the local temperature. The difference is clearly apparent in the disagreement between the observations and the concepts used to analyse them, but it has come to be accepted that much of this should be removed by use of the adjustment parameter microturbulence. It is perhaps worth emphasizing again that this parameter is not a correction factor based on any consideration of the physics involved; it is chosen arbitrarily to force agreement. Is it, nevertheless, possible that microturbulence is an approximation to such a correction factor? Clearly it is not. Microturbulence modifies the absorption coefficient κ_ν , but the real situation departs most from that assumed in that the emission coefficient is not $\kappa_\nu B_\nu(T)$. The correction is to be made in the emission coefficient rather than in κ_ν . This is illustrated by direct analysis (involving no model atmosphere) of the best observed line profiles in the solar spectrum. It is found that the Doppler width is due to thermal motion alone; there is no microturbulence but the emission coefficient is not everywhere given by $\kappa_\nu B_\nu(T)$ (ref. 17) and, at least in the line core, has a different dependence on frequency than κ_ν (ref. 18).

The density of the atmospheres of the giant stars, for which many abundance analyses are carried out, is probably an

order of magnitude lower than the density of the solar atmosphere, and, consequently, local thermodynamic equilibrium is an even weaker assumption. The density in the atmospheres of super-giants is lower again by another factor of about a hundred. The calculation of the line spectrum in radiation emitted from an atmosphere that is not in local thermodynamic equilibrium is very complicated, and no computation has yet been made in which all possible effects are included. There is still disagreement about which effects are significant. In some work, undisputed effects of the breakdown of local thermodynamic equilibrium are taken into account. It is sometimes stated that the results are only insignificantly different, as far as abundance determinations are concerned, from the results obtained assuming local thermodynamic equilibrium, but the latter always include microturbulence so that the comparison is not valid. At present by far the most important question to ask of those who derive stellar abundances is: what is microturbulence?

This question has, of course, been asked before, for example during a meeting in 1960 between astronomers, physicists and aerodynamicists on aerodynamic phenomena in stellar atmospheres¹⁹. The astronomers pointed out that the term microturbulence is an unfortunate misnomer, unjustifiably specifying the nature of the supposed non-thermal motion. But they were emphatic that the apparent extra broadening of absorption lines is due to some kind of velocity field, the characteristics of which remain to be described. It has recently been asserted that the research frontiers in the subject of stellar atmospheres now lie in situations involving hydrodynamics²⁰. It is therefore very important that the concept of microturbulence is now examined more rigorously, especially as there is now some evidence that there is no microturbulence in the solar atmosphere.

The analysis of stellar line spectra must be firmly based in the physics of radiative transfer in a tenuous, hot, optically-thick gas; such a regime can only marginally be investigated experimentally because of the difficulty of achieving, in the laboratory, sufficient optical thickness in a gas of low enough density. The only available test object is the solar atmosphere. It is salutary to realize that the solar line spectrum, the ordinary visual spectrum first investigated by Fraunhofer in 1814, is today reproducible quantitatively only by using two independent adjustment functions, chosen purposefully and without constraint, to force agreement.

¹ Eggen, O. J., Lynden-Bell, D., and Sandage, A. R., *Astrophys. J.*, **136**, 748 (1962).

² Spinrad, H., and Taylor, B. J., *Astrophys. J.*, **157**, 1279 (1969).

³ Cayrel, G., and Cayrel, R., *Astrophys. J.*, **137**, 431 (1963).

⁴ Struve, O., and Elvey, C. T., *Astrophys. J.*, **79**, 409 (1934).

⁵ Cohen, J. G., and Strom, S. E., *Astrophys. J.*, **151**, 623 (1968).

⁶ Parsons, S. B., *Astrophys. J. Suppl.*, **18**, 127 (1969).

⁷ Tomley, L. J., Wallerstein, G., and Wolff, S. C., *Astron. Astrophys.*, **9**, 384 (1970).

⁸ Strom, K. H., *Astron. Astrophys.*, **2**, 188 (1969).

⁹ Smith, M. A., *Astron. Astrophys.*, **11**, 325 (1971).

¹⁰ Spinrad, H., and Taylor, B. J., *Comm. Astrophys. Space Sci.*, **3**, 40 (1971).

¹¹ Deutsch, A. J., in *IAU Symposium No. 26* (edit. by Hubenet, H.), 112 (Academic Press, London, 1966).

¹² Strom, S. E., Strom, K. E., and Carbon, D. F., *Astron. Astrophys.*, **12**, 177 (1971).

¹³ Müller, E. A., Baschek, B., and Holweger, H., *Solar Phys.*, **3**, 125 (1968).

¹⁴ Worrall, G., and Wilson, A. M., *Velocity Fields in Stellar Atmospheres and the Concept of Microturbulence* (to be published in *Vistas in Astronomy* (edit. by Beer, A.) (Pergamon Press, Oxford).

¹⁵ Thomas, R. N., *Non-Equilibrium Thermodynamics in the Presence of a Radiation Field* (University of Colorado Press, Boulder, 1965).

¹⁶ Jefferies, J. T., *Spectral Line Formation* (Blaisdell Publishing Co., Waltham, Mass., 1968).

¹⁷ Curtis, G. W., and Jefferies, J. T., *Astrophys. J.*, **150**, 1061 (1967).

¹⁸ Worrall, G., *Astron. Astrophys.*, **12**, 88 (1971).

¹⁹ *IAU Symposium No. 12* (edit. by Thomas, R. N.), 100 (*Suppl. Nuovo Cim.*, XXII, 1961).

²⁰ Mihalas, D., *Stellar Atmospheres* (W. H. Freeman and Co., San Francisco, 1970).

Stochastic Model for Abnormal Clone Spread through Epithelial Basal Layer

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The induction of a tumour in the basal layer of an epithelium has been simulated by computer. The primary assumption is that tumour growth begins when a single abnormal cell divides faster than surrounding normal cells by a factor K , the "carcinogenic advantage".

THE generative mass in the epithelium is located in the basal layer, above which are differentiated cells, thought to secrete chalone¹, that diffuses back to the basal layer to control cellular divisions. It was thought that when a basal cell divided, one daughter cell remained, while the other was pushed up among the differentiated cells. Leblond *et al.*², however, found that radioactive thymidine remained longer than anticipated in the basal layer, indicating that both daughter cells remained in the basal layer and displaced a neighbouring cell. This sidewise splitting is substantiated by mitotic patterns, tending to cluster in the basal layer.

Bjerknes and Iversen³ have suggested a possible mechanism for tumour induction, in which a basal cell becomes less sensitive to chalone. Since the clone derived from this cell would divide faster than its neighbours, the tumorous cells would push their neighbours out and gradually usurp the entire basal layer.

Cells tend to pack into layers in a honeycomb pattern; sometimes almost perfectly, more often only approximately. Our computer simulations assume a precise honeycomb distribution. We started each realization with a single abnormal cell, which we postulated to divide κ times as fast as the normal cells: we call $\kappa(>1)$ the "carcinogenic advantage". Sometimes, by chance, the entire abnormal clone will be pushed out of the basal layer; the probability of such a regression is $1/\kappa$, and is virtually the only mathematically rigorous result we have obtained.

Computer Simulations

For the complementary situation, where the abnormal clone takes hold, the computer printed out a picture of the basal layer configuration when first there were 100, 400, 900 or 1,600 abnormal cells in this layer. Fig. 1 shows three sequences of such pictures: normal cells are indicated as dots and the abnormal ones as circles (the boundary between normal and abnormal cells has been drawn in). The first column (Fig. 1) shows the situation where κ is so large that the abnormal cell always pushes out the normal one and regression is impossible. Note that from time to time enclaves of normal cells are engulfed by the abnormal, but that the opposite cannot happen. There are no abnormal islands off by them-

selves, as this would require the normal cells to cut off an abnormal peninsula, which cannot happen since the normal cells never win out here.

The middle column (Fig. 1) shows the development of the process when $\kappa=2$. Half the patterns now regress and this sequence of pictures shows one that has taken hold. The enclaves are now larger and take longer to fill in. Also, there are now islands of abnormal cells, notwithstanding the fact that the configuration was started with a single abnormal cell.

The right column (Fig. 1) is particularly instructive. Here $\kappa=1.1$, so that for every series of pictures like this, there will be on average ten that ultimately regress. This sequence looks far more invasive than does that of Fig. 1, which has more the appearance of a carcinoma *in situ*. Our model implies that the infiltrating patterns traditionally associated with cancer growth may be as much due to counter-invasion of the abnormal by the normal cells, as to invasion of the normal by the abnormal cells.

Mathematical Background

In our computer patterns, abnormal cells are often completely surrounded by abnormal cells; if an interior cell divides, an abnormal cell will be pushed out of the basal layer and replaced by another abnormal cell. The configuration in the basal layer will be unaltered, as is the case when a normal cell, entirely surrounded by normal cells, divides. Therefore configuration changes can only occur along the periphery, where abnormal cells exert a thrust of $\kappa-1$ against their normal neighbours. Hence, calling N the total number of abnormal cells and n the number of peripheral abnormal cells,

$$dN/dt = (\kappa - 1)n \quad (1)$$

One would expect n to be proportional to $N^{0.5}$, but it turns out that the dimension that must be assigned to the periphery is not 1, but roughly 1.1, so that the exponent on N becomes 0.55 rather than 0.5. We have been unable to evaluate this quantity mathematically, but there can be no question that it is effectively correct, as indicated by graphs of the expected value of n as a function of N . It is unusual to find fractional dimension^{4,5} arising so naturally in an applied problem. The reason here is apparently that the periphery has an inherent crinkliness, which persists on an absolute scale, while the overall figure is growing in size. What is perhaps more surprising is that the dimensionality of the periphery is independent of κ : for values of κ close to unity, the periphery ought to have been of correspondingly higher dimension. However, an extensive series of realizations, each resulting in a sample of size thirty, indicates that the mean first-passage time to a total of N abnormal cells is given very accurately by the expression

$$\bar{t} = 1.25 N^{0.45} / (\kappa - 1) \quad (2)$$

where the time unit is the mean division time for the normal cells. If we take this to be three diameters, which is in accord

with inferential evidence, and assume that $N=50,000$ results in a clinically manifest growth (measuring some 2 mm in diameter), then with $\kappa=1.1$ this formula yields a mean induction period of over 13 yr for a tumour beginning from a single cell. Even if we assume that the abnormal cells divide twice as fast as the normal, which seems rather extreme, the induction time is still about 1.33 yr.

There exist two other regular tessellations of the plane: by squares and by triangles. We have also examined the spread of abnormal cells through these configurations and the conclusions remain effectively the same, the only difference between

them being the fact that the abnormal cells push out about 20% slower through the square than through the hexagonal lattice, and some 10% slower through the triangular than through the square. The behaviour is clearly a property of the plane itself, rather than the specific lattice in question.

In our simulations, the basal layer is represented by an 80×80 array in the computer memory. To avoid unimportant and tedious boundary effects we have folded the configuration onto a torus, and identified the top, bottom, left and right edges. To render the process Markovian, we have assumed exponential distributions of division times for both normal

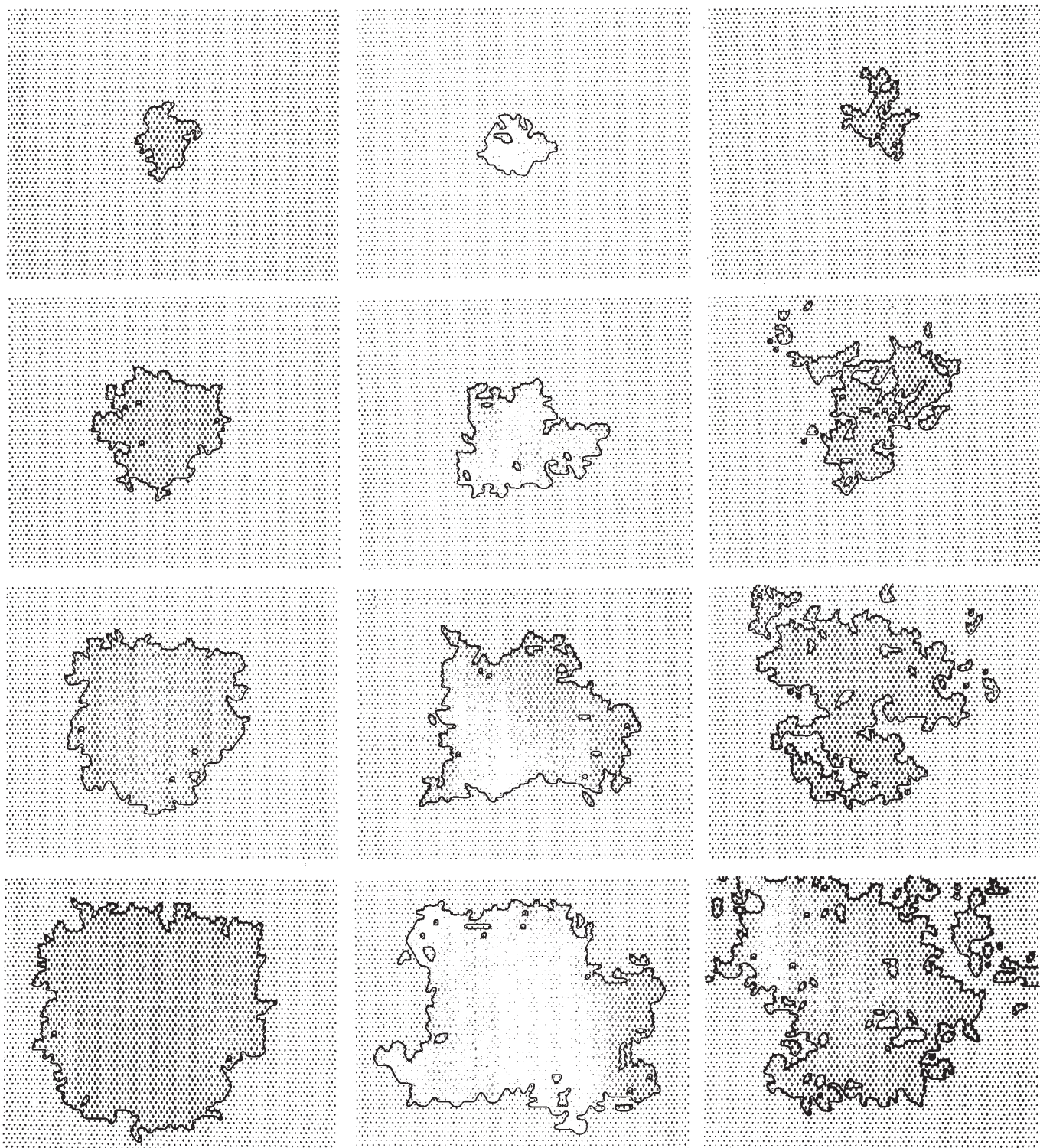


Fig. 1 Configurations of normal and abnormal cells in the basal layer. Abnormal cells, shown as circles, are postulated to divide κ times as fast as normal cells (dots). Cells breed true and, whenever a cell divides, one of the six nearest neighbours, chosen at random, is pushed out so there is room for both daughter cells. The three columns show the configurations when there are, for the first time, 100, 400, 900 and 1,600 abnormal cells. In the left column, $\kappa=\infty$; in the middle, $\kappa=2$; and in the right, $\kappa=1.1$.

and abnormal cells. This makes the probability that a normal cell will divide in the time interval $(t, t + \Delta t)$ equal to Δt , irrespective of the time since its last division. For the abnormal cells, the corresponding probability is $\kappa \Delta t$.

The development of the process in time depends solely on the state of the configuration at one given time. All links joining neighbouring normal and abnormal cells are equally likely to "break" in unit time. The normal neighbour is replaced by an abnormal daughter cell with probability $\kappa/(\kappa + 1)$; with a complementary expression for the probability that the abnormal neighbour is replaced by a normal daughter cell. Such a growth process with $\kappa = \infty$ was considered some years ago by Eden⁶, although he did not have the necessary experimental evidence to recognize it as a possible model for tumour growth. On the strength of limited computer simulations, he made the obvious conjecture that the exponent in equation (2) might be 0.5.

We simulated the process by retaining in the computer memory a list of boundary points and updating this list whenever a change in the configuration took place; adding and deleting as necessary. It was then possible to obtain realizations with κ only slightly greater than unity, which would have been prohibitively time-consuming if we had had to scan the entire array periodically. Solutions of such problems are not strongly dependent on the specific distribution of division times postulated⁷. In particular, the exponent in equation (2) is a consequence of the curious diffuseness of the boundary, which is in no way dependent on the specific distribution assumed.

Critical Discussion

Although we have supposed the carcinogenic advantage to reside in a higher rate of cellular division than normal, one might (O. H. Iversen, personal communication) equally well postulate, for example, that the advantage lay in a stronger

adherence of the abnormal cells to the basement membrane: the conclusions would not be materially changed. The motility of cancer cells is thought to give cancers their invasive appearance, but our contention is that this is not necessary to account for patterns which seem to us to be more evocative of an evenly balanced contest. The same patterns have been adduced as evidence for a multi-cell origin of tumours. Here again, this is unnecessary, although we certainly do not rule them out. Indeed, to harmonize equation (2) with skin-painting experiments on mice, several hundred initial "hits" must be assumed to reduce the latent periods to a reasonable period. This is certainly not an implausible assumption within the experimental limits.

Our model is non-specific; it does not even distinguish between benign and malignant growths. We have studied the basal layer only and have said nothing about subsequent tumour growth. We envisage that any abnormal growth, even a papilloma, requires a broad and substantial foundation in the basal layer.

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¹ Bullough, W. S., and Laurence, E. B., *Proc. Roy. Soc.*, B, **151**, 307 (1960).

² Leblond, C., Messier, B., and Kopriwa, B., *Lab. Invest.*, **8**, 296 (1959).

³ Bjerknes, R., and Iversen, O. H., *Proc. First Intern. Symp. Biokynetik* (edit. by Drischel, H.), 253 (Karl Marx Universität, 1968).

⁴ Hausdorff, F., *Math. Ann.*, **79**, 157 (1918).

⁵ Mandelbrot, B., *Science*, **156**, 636 (1967).

⁶ Eden, M., in *Proc. Fourth Berkeley Symp. on Mathematical Statistics and Probability*, **4**, 223 (University of California Press, 1961).

⁷ Williams, T., *J. Roy. Stat. Soc.*, B, **27**, 338 (1965).

Infall of Matter in Galaxies

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Arguments based on the existence of intergalactic matter are advanced to show that this matter may interact with and be accreted by galaxies to produce observable consequences. The diversity of the phenomena that results from such processes offers a possible understanding of some of the properties of extragalactic systems.

THE most striking result of surveys of the distribution and motions of neutral hydrogen away from the galactic plane¹⁻³ is the discovery of several high velocity hydrogen clouds or concentrations, nearly all having negative (approaching) radial velocities of up to about 200 km s⁻¹. Oort⁴ believes that the clouds represent material of local origin which has left the galactic plane and is being pushed back into it by infalling

intergalactic matter. It seems equally plausible, however, to suppose that we are observing the infalling matter itself, which is initially ionized but recombines into neutral clouds when it is decelerated and compressed by interaction with gas near the galactic plane. Both assumptions lead to similar estimates for the rate of infall of material into the galactic plane. I shall adopt the estimate given by Oort⁴, which is equivalent to a rate of about 25 $M_{\odot}$ pc⁻²/10¹⁰ yr, if the material is 70% hydrogen. If the infall is assumed to occur uniformly over a disk of radius 15 kpc, the total infall rate for our Galaxy is about 2 $M_{\odot}$ yr⁻¹.

This accretion rate requires a fairly high density of intergalactic material outside our Galaxy. There is no conclusive evidence for the existence of intergalactic matter, but several observations suggest its presence. X-ray observations⁵ are consistent with an intergalactic medium having a temperature of about 2-3 $\times 10^6$ K and a density of the order of 10⁻²⁹ g cm⁻³. The spectra of distant quasars often show numerous absorption lines which, according to Silk⁶, can be produced by relatively cool intergalactic clouds with temperatures between 2 $\times 10^4$ and 10⁵ K. There has also been speculation that the "missing

mass" in clusters of galaxies⁷ may be intergalactic matter. In the case of the local group it has been argued^{4,8} that the fact that our Galaxy and M31 are moving toward each other rules out the possibility that the local group could be expanding, and indicates that there must be a substantial amount of intergalactic matter present; Oort⁴ estimates the density of intergalactic matter in the local group to be about $3 \times 10^{-28} \text{ g cm}^{-3}$.

Predicted Accretion Rate

The infall rate to be expected theoretically has been discussed by Oort⁴, and may also be estimated from the classical accretion theories of Bondi and Hoyle⁹ and Bondi¹⁰. According to Bondi, the accretion rate for a galaxy of mass M moving subsonically through a medium of density ρ , gas constant $\mathcal{R}$, and temperature T is given by

$$\frac{dM}{dt} \simeq 2\pi \frac{(GM)^2}{(\mathcal{R}T)^{3/2}} \rho \quad (1)$$

If we adopt $M = 1.5 \times 10^{11} M_{\odot}$ and assume $\rho = 10^{-29} \text{ g cm}^{-3}$ and $T = 2.5 \times 10^6 \text{ K}$, we obtain an accretion rate of only about $0.1 M_{\odot}/\text{yr}$, indicating that accretion is probably not important for galaxies immersed in the general intergalactic medium; if, however, the ambient density is increased to $3 \times 10^{-28} \text{ g cm}^{-3}$, as estimated for the local group, the accretion rate becomes about $2 M_{\odot} \text{ yr}^{-1}$, which agrees with the observationally estimated infall rate for our Galaxy.

Theoretical calculations suggest that the collapse of a protogalaxy¹¹ may leave behind an envelope of uncondensed material which continues to collapse into the central galaxy for a relatively long time. When the boundary of a collapsing protogalaxy is allowed to expand with time, the infall of material from the remnant protocloud can continue at an appreciable rate for well over 10^{10} yr . Infall rates after 10^{10} yr are found to be between 0.4 and $3 M_{\odot} \text{ yr}^{-1}$; again, these numbers agree with the estimated infall rate for our Galaxy. In fact, a much larger range of accretion rates is possible, and in some cases the formation of a galaxy may extend over such a long period of time that even after 10^{10} yr most of the mass remains in the form of uncondensed intergalactic matter.

Galactic Interstellar Medium and Population I Content

According to Oort⁴, the surface density of gas in the galactic plane is $8 M_{\odot}/\text{pc}^2$; the estimated inflow rate of about $25 M_{\odot}/\text{pc}^2/10^{10} \text{ yr}$ is then sufficient to double the amount of gas in the galactic plane after about $3 \times 10^9 \text{ yr}$, if no gas is lost. In reality, however, the gas is continually consumed by star formation. Using a method similar to that of Schmidt^{12,13}, I find values for the rate at which gas is at present being converted into stars in the galactic plane from 15 to $30 M_{\odot}/\text{pc}^2/10^{10} \text{ yr}$. Within the uncertainties, this is the same as the rate at which gas is estimated to be flowing into the galactic plane from intergalactic space, suggesting that the galactic gas and Population I content are being sustained by inflow of material from nearby intergalactic space.

If these estimates are correct, most of the present gas content of our Galaxy has not been present since the Galaxy was formed, but represents material which has been acquired more recently by accretion. This alleviates the problem of understanding how the present gas content of the Galaxy has managed to survive for 10^{10} yr without being consumed by star formation and may also explain why the gas content has been exhausted in some galaxies but not in others which are otherwise quite similar (see below). The dynamical pressure of the infalling material can produce observable perturbations in the motion of the gas in the galactic disk, particularly if the infalling material is clumpy in structure; perturbations of the order of 10 km s^{-1} could then be produced. This might account for some of the deviations from circular motion which have been observed in the galactic interstellar material^{14,15}. Also, the

dynamical pressure of the infalling material is of the same order as that required to trigger the condensation of the interstellar gas into dense, cool clouds¹⁶; thus the infall of matter may be instrumental in producing the observed cloudy structure of the interstellar medium.

Spiral Structure and Hubble Sequence

If the galactic gas and Population I content are continually replenished by the inflow of intergalactic material, the classical "winding up" problem of spiral structure becomes less serious, since the age of the spiral arm material may be considerably less than that of the galaxy itself. When a galaxy acquires new material by accretion, the accreted material will almost inevitably form a spiral pattern, since any clumps or density fluctuations which may be present in it will always be drawn out into spiral arcs by differential rotation. Thus it is possible that the spiral patterns seen in many galaxies may be produced by the accretion of intergalactic material. (It should be noted that even the currently popular density wave theories of spiral structure do not account for the origin of the spiral pattern, which must be generated by some extraneous mechanism.) An almost limitless variety of patterns can be produced by the accretion of clouds of material which differ in size, shape, and angular momentum.

The principal features of the Hubble sequence¹⁷ can also be understood on the hypothesis that spiral arms represent recently accreted material. The only physical property which varies in a strongly systematic way along the Hubble sequence from SO to Sc is the relatively superficial one that the SO galaxies contain no gas or young stars, whereas the spiral galaxies contain gas and young stars in a proportion which increases systematically along the sequence Sa $\rightarrow$ Sc (ref. 18). This can be understood if the SO galaxies represent cases where the collapse of the initial protogalactic cloud took a relatively short time, and the infall of material was completed long ago. The spiral galaxies, on the other hand, may represent cases where, because of less favourable initial conditions, the surrounding intergalactic matter has taken a much longer time to condense, and infall of material is still going on. If the accretion of new material tends to occur sporadically or at a variable rate, a galaxy which has recently experienced active accretion of new material will show a high gas density and a relatively open spiral pattern (Sc), whereas if some time has elapsed since a significant amount of new material was last acquired, the gas content will be partially depleted by star formation, and the arms will be relatively tightly wound (Sa).

Evidence for this interpretation is provided by the correlation of galaxy type with occurrence in clusters. Theoretical collapse calculations¹¹ predict that in a dense cluster of galaxies, where each protogalactic cloud is confined to a relatively limited volume of space, the collapse of a protogalaxy should take much less than 10^{10} yr , and there should be little intergalactic material left at the present time. Most or all of the galaxies in such a dense cluster should then be elliptical or SO galaxies. On the other hand, in a very loose cluster or in the space between clusters, a protogalactic cloud can become much more extended, and its collapse may well take longer than 10^{10} yr ; one should then expect to see many galaxies which are still accreting material, that is, many spiral galaxies. These predictions agree with the fact that the galaxies in massive, dense clusters such as the Coma cluster are nearly all elliptical or SO galaxies, whereas spirals predominate among field galaxies and in small, loose groups such as the Hercules cluster and the local group^{7,19}.

It is possible that some of the barred spirals may represent disk galaxies which have accreted material that happens to be rotating in a plane which is tilted with respect to the disk. Accumulation of material along the line of intersection of the two planes could then produce a "bar" along which the material, having lost much of its angular momentum, falls in toward the nucleus. The radial velocity measures in the barred spiral NGC 1365²⁰ do in fact appear to indicate inflow of material into the nucleus.

Structural and Kinematic Peculiarities

Some galaxies have structural peculiarities which make them difficult, if not impossible, to classify in the Hubble system^{17,21}. It is often difficult to see how the irregularities could be interpreted in terms of a self-sustaining wave pattern, and it is hard to avoid the impression that they are short lived and of relatively recent origin. Also, in many galaxies the gas exhibits substantial deviations from circular motion, often associated with a chaotic or irregular appearance of the galaxy. Examination of photographs of galaxies and of the available kinematic data suggests that in many cases some peculiarities may be caused by infall of intergalactic matter.

For example, NGC 5128—the peculiar galaxy associated with the radio source Cen A—has the appearance of a giant spherical galaxy surrounded by a broad irregular dark band of absorbing material, which may represent material which has recently fallen into the galaxy and is in the process of collapsing to a disk, but has not yet settled into equilibrium. From observations of the radial velocity of the gas in this galaxy, Burbidge and Burbidge²² concluded that the gas and dust in NGC 5128 are moving systematically inward with respect to the stars with a velocity of the order of 100 km s^{-1} . Other studies^{23,24} do not confirm a systematic inward motion, but show nevertheless that large inward velocities are present near the centre of the galaxy; inward velocities of the order of 100 km s^{-1} are observed in 21 cm absorption²³, and up to $\sim 300 \text{ km s}^{-1}$ in H α emission²⁴. All studies agree that large turbulent velocities are present in the gas.

Galaxies with Active Nuclei

In some cases the accreted material may have little or no net angular momentum about the centre of the galaxy; it will then fall directly into the nucleus and become highly condensed in the potential well at the centre of the galaxy. This will lead to a high rate of star formation and a high luminosity in the nucleus of the galaxy, and a strong emission spectrum will be produced by the dense, turbulent gas in the nucleus—as observed in galaxies with active nuclei. Since there is now considerable evidence²⁵ for continuity in the properties of the various types of objects having active nuclei, including the Seyfert galaxies, radio galaxies, and quasi-stellar objects (QSOs), it may be that all are manifestations of nuclear activity caused by rapid accretion of intergalactic material. This possibility has already been suggested by Shklovsky²⁶ as an explanation for radio galaxies.

If a galaxy accretes matter at a “typical” rate of, say, $1 M_{\odot} \text{ yr}^{-1}$, and if the material is transformed into stars as fast as it is accreted, then after about 10^8 yr a nearly constant luminosity of $\sim 10^{10} L_{\odot}$ is attained. An inflow rate of this order, if concentrated in the nucleus of a galaxy, will produce a bright nucleus with a strong emission spectrum. If the galaxy is surrounded by a relatively dense, cool cloud of intergalactic material—for example, with a density of $2 \times 10^{-28} \text{ g cm}^{-3}$ and a temperature of 10^5 K —the accretion rate predicted by equation (1) for a galaxy of mass $10^{11} M_{\odot}$ is about $70 M_{\odot} \text{ yr}^{-1}$, sufficient to produce a luminosity of $\sim 5 \times 10^{11} L_{\odot}$ from normal processes of star formation. Under the same circumstances the accretion rate for a giant elliptical galaxy with a mass of $10^{12} M_{\odot}$ is about $7 \times 10^3 M_{\odot} \text{ yr}^{-1}$, leading to a luminosity of about $5 \times 10^{13} L_{\odot}$, which is comparable with that of QSOs.

Although normal star formation processes may explain, at least in part, the luminosities and the emission spectra of the QSOs, additional mechanisms are required to account for the apparently non-thermal continuous emission, most of which occurs at infrared wavelengths; the variability in luminosity; and the radio emission (also variable) which is sometimes observed. Burbidge and Stein²⁷ have proposed that the continuous spectra of the QSOs and similar objects can be explained by many small non-thermal sources distributed throughout the nucleus of a galaxy; the basic energizing mechanisms for the individual sources might be pulsars or similar objects. Also, Rees²⁸ has recently shown how the radio emission might

be explained by a model in which the energy source is provided by a large number of pulsars or similar objects embedded in a dense disk of gas at the centre of a galaxy. It seems at least energetically feasible that the optical outbursts of the QSOs can be produced by the same basic “flare” mechanism which Rees has proposed to explain the radio outbursts, since the energies involved are of the same order, and are comparable with the gravitational energy available from the formation of a pulsar or other highly collapsed object.

Thus the chief properties of QSOs and similar objects may be accounted for by the formation of large numbers of pulsars in the nucleus of a galaxy where there is a high rate of star formation due to the infall of intergalactic matter. I note that if the primary energy source is gravitational rather than nuclear, the requirements for the accretion theory are somewhat eased, since the gravitational energy available from the formation of collapsed objects may substantially exceed the total nuclear energy available from a given mass of material.

If the QSOs and radio galaxies are indeed explainable by rapid accretion of intergalactic matter, it is tempting to interpret the “jets” observed in the QSO 3C273 and the radio galaxy M87 as “accretion tails” where the infalling material is focused into a narrow wake behind the accreting galaxy, as predicted in classical accretion theories. Such an explanation would account naturally for the highly condensed and collimated nature of these jets, and would allow the optical and radio emissions from the jets to be explained by the same mechanisms which account for the nuclear activity.

I note, finally, that the accretion hypothesis would account readily for the fact, as established from counts of distant quasars, that these objects were more numerous in the past than they are at present²⁹; this would be expected on the basis of the accretion picture, since both the amount and the density of uncondensed intergalactic material would have been higher during the earlier stages of expansion of the universe.

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- ¹ Blaauw, A., Fejes, I., Tolbert, C. R., Hulsbosch, A. N. M., and Raimond, E., in *Radio Astronomy and the Galactic System* (edit. by H. van Woerden), 265 (Academic Press, 1967).
- ² Hulsbosch, A. N. M., *Bull. Astr. Inst. Netherlands*, **20**, 33 (1968).
- ³ Dieter, N. H., *Astron. Astrophys.*, **12**, 59 (1971).
- ⁴ Oort, J. H., *Astron. Astrophys.*, **7**, 381 (1970).
- ⁵ Henry, R. C., Fritz, G., Meekins, J. F., Chubb, T., and Friedman, H., *Astrophys. J. Lett.*, **163**, L73 (1971).
- ⁶ Silk, J., *Astrophys. J.*, **160**, 793 (1970).
- ⁷ Abell, G. O., *Ann. Rev. Astron. Astrophys.*, **3**, 1 (1965).
- ⁸ Kahn, F. D., and Woltjer, K., *Astrophys. J.*, **130**, 705 (1959).
- ⁹ Bondi, H., and Hoyle, F., *Mon. Not. Roy. Astron. Soc.*, **104**, 273 (1944).
- ¹⁰ Bondi, H., *Mon. Not. Roy. Astron. Soc.*, **112**, 195 (1952).
- ¹¹ Larson, R. B., *Mon. Not. Roy. Astron. Soc.*, **145**, 405 (1969).
- ¹² Schmidt, M., *Astrophys. J.*, **129**, 243 (1959).
- ¹³ Schmidt, M., *Astrophys. J.*, **137**, 758 (1963).
- ¹⁴ Münch, G., in *Galactic Structure* (edit. by Blaauw, A., and Schmidt, M.), 203 (University of Chicago Press, 1965).
- ¹⁵ Kerr, F. J., *Ann. Rev. Astron. Astrophys.*, **7**, 39 (1969).
- ¹⁶ Field, G. B., Goldsmith, D. W., and Habing, H. J., *Astrophys. J. Lett.*, **155**, L149 (1969).
- ¹⁷ Sandage, A., *The Hubble Atlas of Galaxies* (Carnegie Institute of Washington, 1961).
- ¹⁸ Sandage, A., Freeman, K. C., and Stokes, N. R., *Astrophys. J.*, **160**, 831 (1970).
- ¹⁹ Burbidge, G. R., and Burbidge, E. M., *Astrophys. J.*, **130**, 629 (1959).
- ²⁰ Burbidge, E. M., Burbidge, G. R., and Prendergast, K. H., *Astrophys. J.*, **136**, 119 (1962).
- ²¹ Arp, H. C., *Atlas of Peculiar Galaxies* (California Institute of Technology, 1966); also published in *Astrophys. J. Suppl.*, **14**, 1 (1966).
- ²² Burbidge, E. M., and Burbidge, G. R., *Nature*, **194**, 367 (1962).
- ²³ Whiteoak, J. B., and Gardner, F. F., *Astrophys. Lett.*, **8**, 57 (1971).
- ²⁴ Sersic, J. L., and Carranza, G., *Info. Bull. Southern Hemisphere*, No. 14, 32 (1969).
- ²⁵ Burbidge, G. R., *Ann. Rev. Astron. Astrophys.*, **8**, 369 (1970).
- ²⁶ Shklovsky, I. S., *Astron. Zh.*, **39**, 591 (1962); English translation in *Soviet Astron.*, **6**, 465 (1963).
- ²⁷ Burbidge, G. R., and Stein, W. A., *Astrophys. J.*, **160**, 573 (1970).
- ²⁸ Rees, M. J., *Nature*, **229**, 312 (1971).
- ²⁹ Schmidt, M., *Astrophys. J.*, **162**, 371 (1970).

LETTERS TO NATURE

PHYSICAL SCIENCES

Deep Sedimentary Basin in the Moray Firth

DURING May and June 1970, the Institute of Geological Sciences (IGS) undertook a seismic reflexion profiling (Sparker) and gravity survey in the Moray Firth along a network of lines spaced approximately 10 km apart. The Bouguer anomaly map shown in Fig. 1 includes the results of the marine gravity survey, land survey results compiled from unpublished IGS data, some unpublished results made available by Drs W. Bullerwell and J. Phemister, and results of a survey published by McGregor and Wilson¹. A previous survey using a sea bed gravity meter has been reported by Collette², whose published map showed a similar pattern of anomalies. The wide and irregular spacing of the stations prevented satisfactory interpretation, however.

The main feature of the present map, and the only one to be discussed here, is the large gravity "low" in the Moray Firth extending north-eastwards into the North Sea. This Collette attributed to the presence of an extensive and thick granitic body at shallow depth. An alternative interpretation, in terms of a deep sedimentary basin, is favoured here, in agreement with a proposal by Hallam³. Doubt was previously cast on Collette's interpretation by the results of aeromagnetic surveys covering the entire region⁴. The magnetic anomalies over the gravity "low" are of a characteristically long wavelength and of relatively low amplitude and are thus consistent with the presence of thick sedimentary cover over magnetic basement. Results of the IGS seismic profiling survey in 1970 show the near surface structure to be that of a sedimentary succession with a regional dip towards the centre of the proposed basin. Subsequent drilling and sampling by IGS⁶ have confirmed the presence of Permo-Triassic, Jurassic and Cretaceous rocks.

A gravity profile A-B (Figs. 1 and 2) has been analysed using a method described by Bott and Young⁷ to calculate the minimum possible density contrast across the margin of the low-density body. Across the northern margin the horizontal gravity gradient is 5.6 mgal/km and a density-contrast of at least 0.17 g/cm³ is required; across the southern margin the horizontal gravity gradient is 8 mgal/km and a density contrast of at least 0.3 g/cm³ is required. Such high gradients and density-contrast values are seldom associated with granitic bodies; however, the area south of B is unusual in that large high-density gabbroic intrusions feature in the surrounding basement geology and gradients of up to 10 mgal/km have been observed over contact zones between granitic and gabbroic bodies¹. Analysis of the gradients at the southern end of line A-B cannot therefore be considered conclusive evidence for the presence of a sedimentary basin. There are no indications of the occurrence of gabbroic bodies at the northern end of the profile. Since density contrasts between granite and meta-sedimentary country rocks of more than 0.17 g/cm³ have not been observed in Britain⁷ the evidence for the existence of a sedimentary basin beneath this part of the profile is stronger. A significant discovery of the present survey is that the zones of highest gradient are all along well developed linear features indicating large faults as marginal control of the low density body. Thus, there is seen to be strong evidence for the occurrence of a deep sedimentary basin.

To determine the depth of the basin, profile A-B has been

interpreted using a two-dimensional model (Fig. 2). A linear regional field based on Bouguer anomaly values observed at either end of the profile was removed. A density of 2.7 g/cm³ is assumed to be representative of the Middle Old Red Sandstone and Dalradian rocks enclosing the basin on the north and south respectively and a mean density of 2.3 g/cm³ is assumed for the Permian and Mesozoic rocks in the basin, these values being based on published density determinations^{1,4,8} for such rocks as are found on land in the area. The model fitted to the data thus assumes a density contrast of -0.4 g/cm³ except near A where a wedge of denser sediment is postulated in order to explain the steady decrease of anomaly level as the basin is approached. Seismic profiles show that Mesozoic rocks do not reach the coastline in this area and it was concluded that upper Old Red Sandstone probably occurs here, the mean density being similar to that found by McQuillin⁸ in the Orkneys (2.41 g/cm³). Drilling in this area has recently confirmed this.

The model structure (Fig. 2) shows that along A-B the depth of the basin probably does not exceed 4 km. Alternative models based on a higher density contrast or a lower regional field would give lower depth values but it is thought unlikely that the

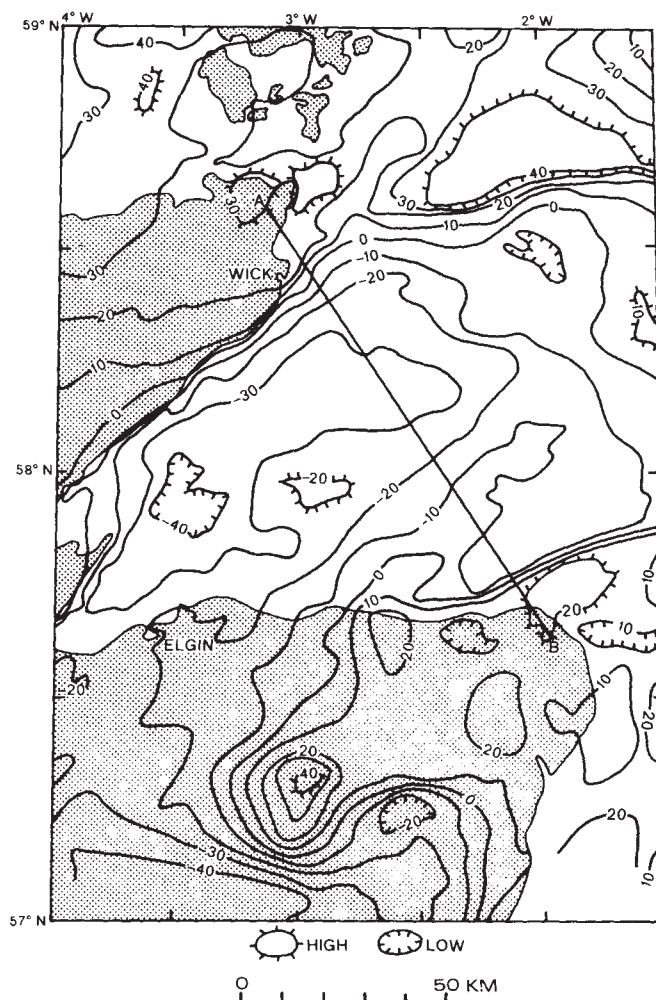


Fig. 1 Bouguer anomaly map of the Moray Firth. Contour interval 10 mgal; assumed density 2.67 g/cm³.

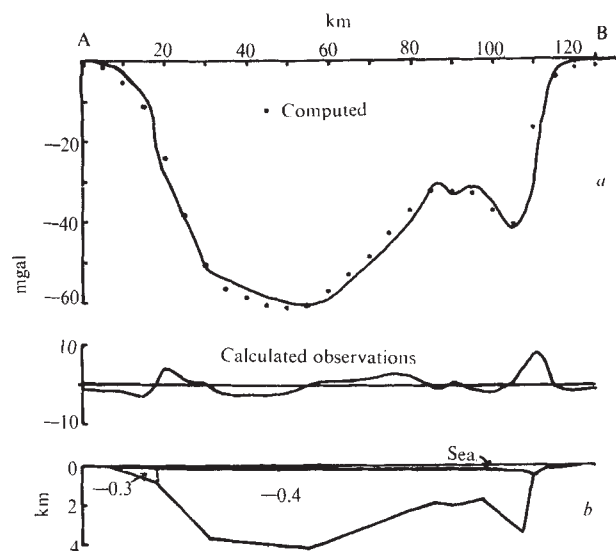


Fig. 2 a, Residual anomaly profile along A-B; b, structural model, with density contrasts in g/cm³.

maximum depth of the basin would be less than 3.5 km or more than 4.5 km. The basin is clearly fault controlled, a dip of 50° being deduced in the model for the southern margin, the boundary coinciding with a long narrow submarine trench in places exceeding 200 m in depth. Further steep gradients indicate major faults on northern and north-western margins; the north-western one is along the seaward continuation of the Helmsdale Fault line.

The basin appears to shallow slowly to the east, there being no clearly defined eastern margin. Bouguer anomalies are lowest north of Elgin. The regional field is, however, lower in this region than along profile A-B, the residual anomalies are of similar magnitude and the maximum depth of the basin here is unlikely to exceed 4 km. Within the area interpreted as a basin, the gravity field shows secondary features indicating secondary structural effects; for example on the profile A-B, towards the southerly end of the section, a basement ridge is indicated. Density changes in the basement may partially be the cause but the marine gravity data do not resolve this problem.

Finally, it is worth noting that the presumed seaward extension of the Great Glen Fault line is not marked by a gravity gradient. This is not surprising. On the adjacent land, gravity gradients associated with the fault are small and at sea the structure is covered for most of its length by a substantial thickness of Mesozoic rocks. Some evidence for its location has been found on seismic profile records supporting previous arguments that the fault has been reactivated since the Mesozoic⁹.

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¹ McGregor, D. M., and Wilson, C. D. V., *Quart. J. Geol. Soc. Lond.*, **123**, 99 (1967).

² Collette, B. J., *Gravity Expeditions 1948-58*, 5, Part 2 (Delft University Press, 1960).

³ Hallam, A., *The Geology of Scotland* (edit. by Craig, G. Y.), 414 (Oliver and Boyd, 1965).

⁴ Fenning, P., in *The Geology of the Elgin District*, Appendix III (HMSO, 1968).

⁵ Institute of Geological Sciences, *Aeromagnetic Map Sheets 13 and 14* (1968).

⁶ Chesher, J., *Marine Drilling by M. V. Whitethorn in Scottish Waters 1970-71* (IGS, in the press).

⁷ Bott, M. H. P., and Young, D. G. G., *Quart. J. Geol. Soc. London*, **126**, 413 (1971).

⁸ McQuillin, R., *Institute of Geological Sciences Geophysical Paper No. 4* (1968).

⁹ Holgate, N., *Scott. J. Geol.*, **5**, 97 (1969).

Terrestrial Age of Nineteen Stony Meteorites derived from their Radiocarbon Content

THE effects of cosmic radiation on meteorites have been studied thoroughly during the past 15 yr.^{1,2} ¹⁴C is chiefly produced by three nuclear reactions: ¹⁴N(n,p)¹⁴C, ¹⁶O(p,3p)¹⁴C and ¹⁶O(n,2pn)¹⁴C. The first reaction occurs in the Earth's atmosphere³⁻⁴ and provides the basis for the well known radiocarbon dating method. The ¹⁴N(n,p)¹⁴C reaction has its largest cross-sections (σ=1.7 bar) in the thermal neutron energy region. The ¹⁶O spallation reactions (σ=2 mbar) require energies above 10 MeV. The air mass of 1 kg cm⁻² above the surface of the Earth dissipates most of the energy of the primary cosmic rays. Therefore, ¹⁴C production in rocks on the Earth's surface is negligible. The surface of an object in space, however, is exposed to the full flux of the primary cosmic radiation. Meteorites, therefore, contain a measurable amount of high-energy spallation products. Meteorites contain very little nitrogen, and hence the ¹⁴C production is dominated by ¹⁶O spallation. The equilibrium ¹⁴C activity in stony meteorites per unit weight has a different value from that of the terrestrial atmosphere. The approximate average values for the ¹⁴C production rate are 120 ¹⁴C atoms min⁻¹ cm² at the Earth's surface (containing 1 kg of air) and 60 ¹⁴C atoms min⁻¹ kg of meteorite⁵.

Finds usually show substantially higher oxygen values than falls, a fact which can be attributed to weathering. The variation in oxygen content makes it difficult to normalize the ¹⁴C activity of finds to their pre-fall oxygen content. But oxygen variations alone do not account for the variations in the ¹⁴C activity. From observations on lunar material (rock 1202) a considerable depth gradient can be expected⁶⁻⁸. Surface ablation caused by air friction during passage of a meteorite through the atmosphere can account for a loss of as much as 10 cm. Parts of a meteorite may reach the surface of the Earth nearly unablated.

The location of a specimen from a find is always uncertain. Therefore, an intrinsic uncertainty of the age values of ±2,000 yr has to be assumed, in addition to the experimental errors. Further possible variations of the ¹⁴C activities arise from differences in the pre-terrestrial orbital parameters.

Roughly 10 g of meteorite samples was crushed and mixed in a porcelain crucible with 60 g of V₂O₅. The crucible was placed in a stainless steel vessel and evacuated for several hours at a temperature of 100° C. Oxygen (20 cm in pressure) was introduced into the vessel and the temperature was raised to 800° C, where it was maintained for four hours. After 3.5 h of heating, the gases were circulated for 30 min using a Toepler pump. During circulation, the gases passed through a CuO furnace, dry-ice-acetone traps, and traps cooled with liquid nitrogen. The non-condensed gases were then removed, the liquid nitrogen dewars replaced with dry-ice-acetone coolants, and the CO₂ collected. As only approximately 60 cm³ of CO₂ was obtained from the meteorites, CO₂ was added for a total volume of 200 cm³ STP. The CO₂ was converted into acetylene⁹ by the reaction



The overall yield of acetylene was 80±5%.

After the acetylene had been aged for 3 weeks to allow any ²²²Rn (t_{1/2}=3.6 d) present to decay, the acetylene was counted in a 100 cm³ proportional counter constructed at the University of Berne. A two-channel anticoincidence system was used. The two discriminators were set to correct for any drift, so that all samples could be counted with the same gas gain, varying counter gas pressures. Blank samples were prepared for each jar of V₂O₅ used. Blank counting rates agreed within statistical error with the background counting rates. The background gas, obtained by burning anthracite and converting the CO₂ into acetylene, had a counting rate of 0.690±0.013 i.p.m. The counter efficiency was determined

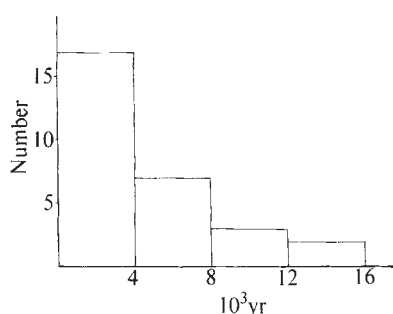


Fig. 1 Number of meteorite finds against their age on Earth.

using the NBS oxalic acid ^{14}C standard and was found to be 70.1%.

Results of the measurements are listed, and terrestrial ages are given, in Table 1. The ^{14}C value of the four falls analysed averages 57.3 d.p.m./kg. Suess and Wänke¹⁰ found an average of 48.2, and Goel and Kohman⁵ 63.7 d.p.m./kg. The results are in fair agreement. The high value of specimens taken approximately 5 mm below the crust of the carbonaceous chondrite Allende is surprising. The mean oxygen content of the three types of carbonaceous chondrites was found by Vogt and Ehmann¹¹ to be 41%, only 10% higher than in ordinary chondrites. The ^{14}C value of the crust of Allende (64.3 d.p.m./kg) agrees well with that of the other meteorites. There is a remote possibility that the value obtained for the deeper layers of this meteorite (108 d.p.m./kg) might be attributed to contamination. Perhaps the low surface value can be explained as a loss of ^{14}C resulting from heating during the fall of the meteorite to Earth.

The average of 57.3 d.p.m./kg for falls demonstrated the 4π irradiation geometry of meteorites in space, but the Moon, a much larger object, has a 2π irradiation geometry for galactic rays indicated by the value of 26.7 d.p.m./kg^{6,12}.

The results show that the average age of the investigated stony meteorites is 5,200 yr. The set of finds used for the investigation was a more or less random selection of specimens

Table 1 The ^{14}C Content of Meteorites and the Terrestrial Ages of Finds

Meteorite	Place and year of fall or find	^{14}C d.p.m./kg	Terrestrial age (yr)
Falls			
Allende	Mexico, 1969		
Crust		64.3 ± 4.3	—
5 mm below crust		108.0 ± 6.4	—
Bruderheim	Alberta, 1960	56.5 ± 5.0	—
Peace River	Canada, 1963	68.2 ± 5.1	—
Richardton	North Dakota, 1918		
Crust		36.5 ± 3.1	—
5 mm below crust		44.2 ± 2.8	—
Finds			
Alamogordo	New Mexico, 1938	31.7 ± 2.4	5,000 ± 2,600
Bluff	Texas, 1878	35.9 ± 2.7	3,900 ± 2,600
Brownfield	Texas, 1937	12.2 ± 2	12,700 ± 4,500
Clovis	New Mexico, 1961	66.4 ± 5.0	2,000 ± 2,000
De Nova	Colorado, 1940	20.6 ± 2	8,300 ± 3,000
Densmore	Kansas, 1879	38.6 ± 2.9	3,500 ± 2,500
Dimmit	Texas, 1947	37.5 ± 2.7	3,800 ± 2,600
Elm Creek	Kansas, 1906	49.6 ± 3.7	1,200 ± 2,000
Estacado	Texas, 1883	24.3 ± 2	6,800 ± 3,000
Faucett	Missouri	58.1 ± 4.4	2,000 ± 2,000
Gilgoin	New South Wales, 1889	37.8 ± 2.9	3,500 ± 2,500
Keyes	Oklahoma, 1939	41.4 ± 3.1	2,700 ± 2,000
Kingfisher	Oklahoma, 1950	48.1 ± 3.1	1,600 ± 2,000
Ladder Creek	Kansas, 1937	36.5 ± 2.7	3,800 ± 2,600
Leon	Kansas	18.1 ± 2	9,200 ± 3,100
McKinney	Texas, 1870	16.5 ± 2	10,200 ± 3,500
Texline	Texas, 1937	26.3 ± 2	6,400 ± 3,000
Tulia	Texas, 1917	26.4 ± 2	6,400 ± 3,000
Weldona	Colorado, 1934	24.9 ± 2	6,800 ± 3,000

from the collections of the National Museum of Natural History and the Center for Meteorite Studies of the Arizona State University (Nininger Collection) and therefore this value may well represent the average terrestrial age of finds of ordinary chondrites in the western USA. A referee has drawn my attention to the fact that carbonaceous chondrites and achondrites weather more rapidly, and that the specimens examined were all from a part of the world with a fairly low rainfall. The observed ages represent the terrestrial life of ordinary chondrites under the climate of the western United States. It would be interesting to compare these results with those for specimens from a more humid climate, where the rate of weathering is probably considerably greater. From the age histogram shown in the figure a terrestrial "half life" of ordinary chondrites until they disintegrate by weathering under the climatic conditions of the western United States and are no longer recognized can be estimated to be about 3,600 yr.

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- Honda, M., and Arnold, J. R., *Handbuch der Physik*, 46/2, 613 (1967).
- Arnold, J. R., Honda, M., and Lal, D., *J. Geophys. Res.*, 66, 3519 (1961).
- Lingenfelter, R. E., *Rev. Geophys.*, 1, 35 (1963).
- Libby, W. F., *Radiocarbon Dating* (University of Chicago Press, 1955).
- Goel, P. S., and Kohman, T. P., *Science*, 136, 875 (1962).
- Boeckl, R. S. (in the press, 1971).
- Shedlovsky, J. P., Honda, M., Reedy, R. C., Evans, J. C., Lal, D., Lindstrom, R. M., Delany, A. C., Arnold, J. R., Loosli, H. H., Fruchter, J. S., and Finkel, R. C., *Science*, 167, 574 (1970).
- Finkel, R. C., Arnold, J. R., Reedy, R. C., Fruchter, J. S., Loosli, H. H., Evans, J. C., Shedlovsky, J. P., and Delany, A. C., *Second Ann. Lunar Science Conference* (Houston, 1971).
- Hubbs, C. L., and Bien, G. S., *Radiocarbon*, 9, 261 (1967).
- Suess, H. E., and Wänke, H., *Geochim. Cosmochim. Acta*, 26, 475 (1962).
- Vogt, J. R., and Ehmann, W. D., *Radiochim. Acta*, 4, 24 (1965).
- Wänke, H., Begeman, F., Vilček, E., Rieder, R., Teschke, F., Born, W., Quijano-Rico, M., and Wlotzka, F., *Science*, 167, 523 (1970).

Transfer by Aerosols of Effects of High Energy Solar Radiation to the Biosphere

THE essential role of the atmosphere in making life possible by excluding from the biosphere high energy radiation, particularly the solar ultraviolet, has long been appreciated. However, a pathway for the indirect transfer of radiation injury to air-breathing animals exists because the stratospheric aerosol layers are exposed to high solar ultraviolet intensities. These particles eventually descend into the lower atmosphere adjacent to the Earth's surface.

Recent measurements of aerosol concentration in the stratosphere, reviewed by Rosen¹, have confirmed the ubiquity of rather sharply defined layers of 0.01 to 1.0 μm particles at approximately 20 km altitude. Fig. 1, adapted from Rosen², shows how the aerosol concentration falls below the tropopause, then rises abruptly near ground level to the much higher aerosol densities which characterize the turbulent surface exchange layer comprising about the first km above ground.

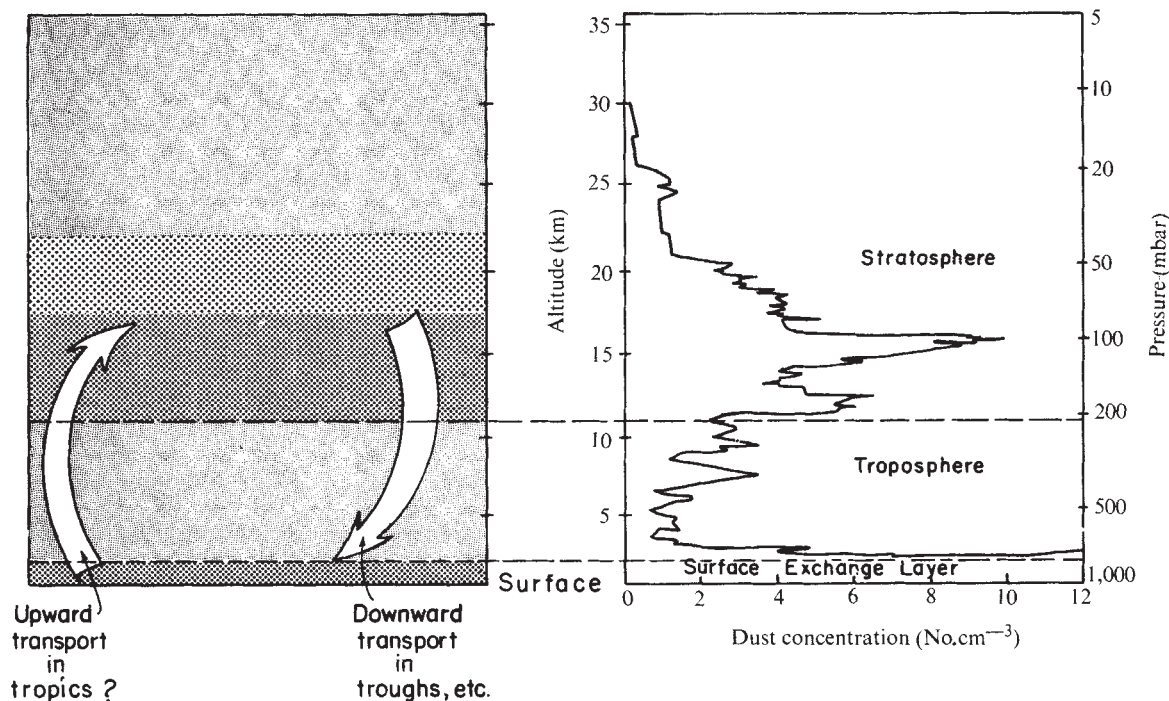


Fig. 1 Aerosol concentration in the Earth's atmosphere.

The composition of the stratospheric aerosols is still not completely determined. Junge³ has proposed ammonium sulphate particles but siliceous dusts, volcanic debris, combustion products, sea salt and polymerized terpene⁴ particles are all expected to be present. I assume that a substantial fraction of the aerosol is organic. This is not excluded by the available data.

Because the stratospheric aerosols cluster near the lower edge of the ozone layer, little ultraviolet penetrates in the wavelengths 220 to 300 nm. Below 200 nm oxygen absorption is almost complete, but the band 200 to 220 nm opens a partial window. At an altitude of 20 km at the equator, solar ultraviolet penetrates a minimum air mass of 0.44 km-atmospheres STP (ref. 5). The irradiation shown in Fig. 2 is the only significant energy shortward of optical wavelengths⁵⁻⁷. Fig. 2 also shows the cross section per molecule for the inactivation of dry trypsin⁸. This is representative of the action spectra⁹ of ultraviolet for effecting biochemically significant changes.

I consider a uniform film of dry trypsin, 0.01 mg cm^{-2} —roughly $0.1 \text{ }\mu\text{m}$ thick—as a model for the effects of ultraviolet on aerosols. The incident flux in the 210 nm window will inactivate 1.5×10^8 molecules $\text{cm}^{-2} \text{ s}^{-1}$, giving a lifetime against complete inactivation of $1.7 \times 10^6 \text{ s}$ of irradiation. The dose rate is equivalent in this effect to 21 rad s^{-1} of γ -radiation with $G=1.2$ per 100 eV (ref. 10). I distinguish the irradiated, organic aerosols by the name "aerons".

It has been demonstrated¹¹ that the radioactivity produced in nuclear weapons tests usually attaches indiscriminately to natural aerosols as it percolates downward through the stratosphere, ultimately re-entering the troposphere and appearing as fallout. The mechanisms¹²⁻¹⁴ which cause fallout aerosols to exchange from the stratosphere to the troposphere will similarly transport aerons into the lower atmosphere. I expect aeron concentrations in surface air to show the slow seasonal and marked day-to-day variations exhibited by radioactive fallout. Coagulation³ of aerons with the larger and more plentiful surface-air aerosols (for example, industrial pollutants, pollens) will cause the aerons to grow towards the size (0.1 to $0.3 \text{ }\mu\text{m}$) optimum for deposition in the deep alveolar regions of the lungs.

We can estimate the aeron concentration to be expected in surface air. Pilipowskyj *et al.*¹⁵ have estimated the aerosol mixing ratio between 18 and 23 km over Miami, Florida, in

April 1965 to exceed $(6 \pm 2) \times 10^{-7} \text{ g/g}$, corresponding to a minimum mass of $2.6 \times 10^{-5} \text{ g/(cm}^2 \text{ column)}$. Fallout studies have shown¹⁶ that transfer of the total stratospheric radioactivity to the troposphere has a time constant of $\sim 1.6 \text{ yr}$. Roughly 90% of fallout penetrates the lower atmosphere in rainwater, the rest appearing as an aerosol with a lifetime of $\sim 30 \text{ days}$ ³. Assuming that aerons constitute half the stratospheric aerosol, we estimate $7.6 \times 10^{-8} \text{ g/(cm}^2 \text{ column)}$ for the mass burden of the troposphere. This will be distributed over the surface exchange layer with a scale height³ of $\sim 800 \text{ m}$,

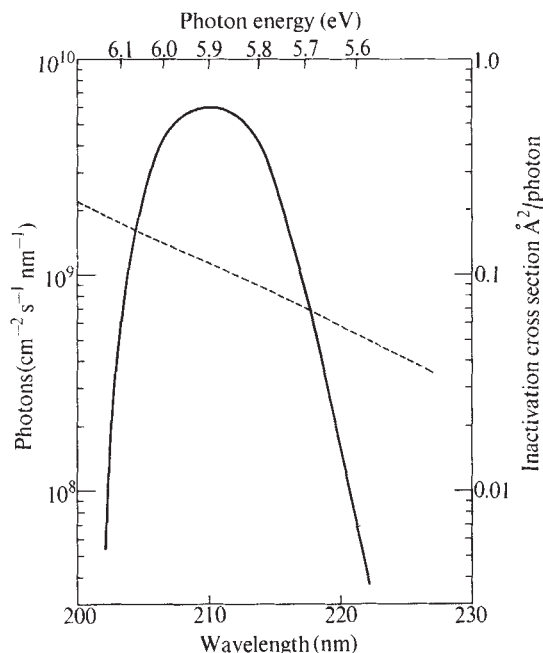


Fig. 2 Solar irradiation compared with cross section per molecule for inactivation of dry trypsin⁸. The absorption cross section is 10 to 100 times larger, but is insufficient to attenuate the radiation over the dimensions of interest ($\sim 0.1 \text{ }\mu\text{m}$). We may therefore measure the flux in rads. The solar ultraviolet flux is $0.005 \text{ erg mm}^{-2} \text{ s}^{-1}$ of $\sim 6 \text{ eV}$ photons. —, Solar spectrum at 20 km; equator, vertical incidence; ---, dry trypsin inactivation cross section⁸.

leading to an average aeron concentration in the surface air¹⁷ of $\sim 1 \mu\text{g m}^{-3}$.

Although radiotoxins and the whole question of indirect (chemically transferable) radiation injury to cells have been a subject of controversy in the past, it is now widely accepted that^{18,19} radiation damage can be produced both directly and indirectly (for example, by the production of disruptively reactive compounds, such as free radicals or peroxides, both inside and outside the cell). Human and animal food is known to become toxic when given very high doses of radiation, notwithstanding the many opportunities for detoxification which arise during the process of digestion and absorption²⁰. But little work has been carried out on the toxicity of radiation products administered to mammals by more direct routes, such as injection or inhalation.

One study is available on the effects of the injection of irradiated plant material into animals. Mel'nikova and Kopylov²¹ irradiated potatoes and injected an extract intramuscularly into mice. This produced weight losses over two days which were comparable with the weight loss of mice, otherwise untreated, which received direct γ -radiation. Experiments in rats at lower doses displayed the abrupt fall in leucocyte counts characteristic of whole body irradiation or poisoning by radiomimetic drugs.

From the data of ref. 21 we may compute the efficiency of the potato extract in transferring the morbid effects of radiation. The mass of potato tissue injected into each mouse was 0.57 g and this had absorbed 8,600 g rad or 0.86×10^6 erg during the original irradiation, 34×10^3 erg g⁻¹ of body weight of the mouse. The control mice suffered similar symptoms after receiving 700 rad whole-body γ -irradiation or 70×10^3 erg g⁻¹ body weight. It seems that the efficiency of transfer of these particular toxic effects of radiation by means of an irradiated intermediate exceeds 100%; it will be taken to be 100% for the effects discussed below.

Because the aerons received large (megarad) doses of ultraviolet, saturation effects will limit the ultimate concentration of radiotoxic materials. Electron spin resonance (ESR) studies²² of natural materials during irradiation have disclosed saturation beginning at doses of about 1 mrad. The final, stable spin states are believed to be caused by peroxy radicals and similar reactive species; they have lifetimes of at least months. In most dry materials near 300 K the maximum density of stable spins is $\sim 10^{19}$ g⁻¹, corresponding to the rather substantial stored radiation dose of 7×10^8 erg g⁻¹ or 7 g mrad g⁻¹.

Adopting 7×10^8 erg g⁻¹ for the energy transfer capacity of the aerons and multiplying by the concentration of $1 \mu\text{g m}^{-3}$, we find that normal surface air will transfer 7×10^{-4} erg cm⁻³ of equivalent radiation energy. This exceeds by a factor of $\sim 10^9$ the primary cosmic ray energy density.

The International Commission on Radiological Protection has adopted 20 m³ as the daily air inspiration of an adult, and a model for deposition of small aerosols in the lung which requires 25% of soluble material to be deposited in the lung and absorbed. In view of the uncertainties about the composition of aerons, one can hardly aver to their solubility; however, it has been postulated that they are composed of biological material and because their size will encourage phagocytosis we may expect ultimate lysozymal digestion.

Thus we arrive at an estimate for the energy transferred to an adult human by aerons: 3.5×10^3 erg day⁻¹. Distributed over the blood of a 70 kg man, this represents about 7 mrad day⁻¹ or 2.5 mrad yr⁻¹. Alternatively, distributed over the entire body weight it is equivalent to 0.5 mrad day⁻¹, 180 mrad yr⁻¹; this is roughly twice the average natural background radiation dose from all causes. There are many points of uncertainty in the above argument which must be reflected in the unreliability of the final estimate of dose, but to the extent that a lower limit was used for the aeron mass burden in the stratosphere, this estimate is itself biased towards underestimation.

Another set of arguments tends to implicate some quality

of stratospheric air in many epidemic illnesses. For example, Tromp²³ has reviewed the evidence associating the passage of cold fronts with onset or exacerbation of an extraordinary variety of illnesses; Danielsen¹² has established that cold fronts are normally associated with substantial influxes of stratospheric air to the lower atmosphere. There is also an average annual variation in stratosphere-troposphere exchanges which shows a mid-latitude maximum in later winter-early spring, coincidental with the major peak²³ in respiratory disease incidence which has so far eluded convincing explanation.

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- ¹ Rosen, J. M., *Space Sci. Rev.*, **9**, 58 (1969).
- ² Rosen, J., *J. Geophys. Res.*, **73**, 479 (1968).
- ³ Junge, C. E., *Air Chemistry and Radioactivity* (Academic Press, New York, 1963).
- ⁴ Went, F. W., *Tellus*, **18**, 547 (1966).
- ⁵ Howard, J. N., King, J. I. F., and Gast, P. R., *Thermal Radiat.*, in *Handbook of Geophysics*, ch. 16 (Macmillan, New York, 1960).
- ⁶ Thekaekara, M. P., and Drummond, A. J., *Nature Physical Science*, **229**, 6 (1971).
- ⁷ London, J., in Urbach, F., editor, *The Biologic Effects of Ultraviolet*, 335 (Pergamon, Oxford, 1969).
- ⁸ Setlow, R., and Doyle, B., *Biochim. Biophys. Acta*, **24**, 27 (1957).
- ⁹ McLaren, A. D., and Shugar, D., *Photochemistry of Proteins and Nucleic Acids* (Pergamon Press, Oxford, 1964).
- ¹⁰ Hutchinson, F., and Watts, E., *Radiat. Res.*, **14**, 803 (1961).
- ¹¹ Martell, E. A., *Tellus*, **18**, 486 (1966).
- ¹² Danielsen, E. F., *J. Atmos. Sci.*, **25**, 502 (1968).
- ¹³ Dingle, A. N., *Science*, **148**, 227 (1965).
- ¹⁴ Miyake, Y., Saruhashi, K., and Katsuragi, Y., *J. Radiat. Res. Tokyo*, **3**, 148 (1962).
- ¹⁵ Pilipowskyj, S., Weinman, J. A., Clemesha, B. R., Kent, G. S., and Wright, R. W., *J. Geophys. Res.*, **73**, 7553 (1968).
- ¹⁶ Fabian, P., Libby, W. F., and Palmer, C. E., *J. Geophys. Res.*, **73**, 3611 (1968).
- ¹⁷ Swinnerton, J. W., Lamontagne, R. A., and Linnenbom, V. J., *Science*, **172**, 943 (1969).
- ¹⁸ Kuzin, A. M., *Radiation Biochemistry*, Israel Prog. for Scientific Translations, Jerusalem (1964), translated from *Radiatsionnaya Biokhimiya*, Izdatel'stvo Akademii Nauk SSSR, Moscow (1962).
- ¹⁹ Scott, D., *Cell Tissue Kinet.*, **2**, 295 (1969).
- ²⁰ Schubert, J., *Bull. World Health Org.*, **41**, 873 (1969).
- ²¹ Mel'nikova, S. K., and Kopylov, V. A., in *Radiotoxins* (edit. by Kuzin, A. M.) (US Dept. Commerce, National Technical Information Service, Springfield, Virginia, document AD691870, 1968); translated from *Radiotoksiny* (Atomizdat, Moscow, 1966).
- ²² Dodd, N. J. F., and Ebert, M., *Intern. J. Radiat. Biol.*, **18**, 451 (1970).
- ²³ Tromp, S. W., *Medical Biometeorology* (Elsevier, Amsterdam, 1963).

BIOLOGICAL SCIENCES

Association of Antibodies to Australia Antigen with Anti-Gm Antibodies in Italian Patients with Thalassaemia

THERE is considerable evidence that Australia antigen (Au(1)) is intimately associated with an infectious agent that can cause hepatitis in man¹. From the time of our original discovery of Au(1)² we have also tested the hypothesis that it has the properties of a serum protein polymorphism. This hypothesis has been supported by population, genetic, chemical and immunological studies. Because the two hypotheses are not

mutually exclusive, we have combined them to form a third hypothesis, namely that Australia antigen is an infectious agent which causes hepatitis in man and has many of the properties of a serum protein polymorphism³. Here we report observations on patients with thalassaemia that bear on this concept.

Thalassaemia patients receive transfusions beginning early in life and are exposed to many serum proteins and other blood constituents which are different from their own. Seven years ago, Vierucci and his colleagues started a systematic study of thalassaemia patients from Ferrara and other sections of North Italy. The focus of these investigations has been on the Ag (lipoprotein) system, anti-Ag, red cell and white cell antigens and antibodies, and their relations to age, sex, morbidity, mortality and treatment⁴. As a part of this combined study the frequencies and distribution of Au and anti-Au(1), Gm and anti-Gm were investigated; the results are reported here. We found a significant association between antibodies to Au(1) and antibodies to Gm groups. The hypotheses generated by these findings will also be discussed.

One hundred and sixty-nine thalassaemia patients were included in the overall study. This included all the regular patients (143) seen at Centro della Microcitemia di Ferrara, twenty-one from the paediatric clinic of the University of Ferrara and five patients seen in the paediatric clinics in Siena and Florence. Of these, there were 123 on whom both anti-Au and anti-Gm were determined. In another paper we have shown that if a thalassaemia patient has Australia antigen at one point in time he will nearly always have it when tested subsequently⁵. If he has anti-Au(1), this is also (in general) persistent. That is, persistent Au(1) or anti-Au(1) is characteristic of an individual and the patient does not shift from the persistent Au(1) "type" to the anti-Au "type", or vice versa.

Anti-Gm was determined by the method used by Ropartz *et al.*⁶. Most of the sera classified as anti-Gm are anti-Gm(1). A modification of the immunodiffusion method of Blumberg and Riddell⁷ was used for the determination of Au(1) and anti-Au(1). The results of the study were compared by the use of a 2×2 contingency table and the chi square with small number correction used for determining the probabilities.

Table 1 Anti-Gm in Thalassaemia Patients

	N	Anti-Gm	%	Probability
Anti-Au(1)	30	22	73.3	$\chi^2 = 5.3892$ $P = 0.0203$ $\chi^2 = 6.8606$ $P = 0.0088$
Au(0)*	76	35	46.1	
Au(1)	17	5	29.4	
Total	123	62	50.4	

* These individuals had neither Au(1) nor anti-Au(1).

There were thirty patients with anti-Au(1). Of these, twenty-two (73.3%) also had anti-Gm (Table 1). This is significantly higher than the frequency of anti-Gm in the patients who had persistent Au(1) in their blood (five of seventeen, 29.4%; $P = 0.0088$). It is also significantly greater than the frequency of anti-Gm in patients who have neither Au(1) nor anti-Au(1) (thirty-five of seventy-six, 46.1%; $P = 0.0203$).

Based on these observations we made a further hypothesis which derived from the infectious agent-polymorphism concept. If Australia antigen has the properties of a polymorphism and contains, or is closely associated with, the Gm groups, antibody formation to both Gm and Au(1) would be more common in patients who lack Gm phenotypes. The Gm specificities (Gm 1, 2, 4, 5, 10, 11, 21) of twenty-four patients with anti-Au(1) and eleven patients with persistent Australia antigen were determined. From Table 2 the frequency of Gm types is always greater in thalassaemia patients who have developed persistent Australia antigen than in those who have developed anti-Au(1), a finding consistent with the hypothesis. These observations

should be repeated in other populations to continue to test the validity of this hypothesis.

At about the same time these studies were in progress, Millman *et al.*⁸ produced a report on the chemical characteristics of Australia antigen. The antigen was isolated from peripheral blood and purified by column separation, density gradient sedimentation, and proteolytic digestion of any remaining serum proteins. The purified material (which did not contain any serum protein which could be identified by immunological methods) was treated with the detergent 'Tween 80'. The released products included serum proteins, namely gamma globulin (both heavy and light chain), albumin, lipoprotein and complement; that is, the agent associated with Australia antigen contains serum protein. We are now testing the hypothesis that these proteins including the gamma globulins are polymorphic. If this hypothesis is supported, then it could explain individual inherited differences in developing antibody, persistent antigen and disease.

Table 2 Gm Types in Thalassaemia Patients

	Au(1) (N=11)		Anti-Au(1) (N=24)	
	+	%	+	%
Gm(1)	7	63.6	9	37.5
Gm(2)	1	9.1	1	4.2
Gm(4)	11	100.0	21	87.5
Gm(5)	10	90.9	21	87.5
Gm(10)	10	90.9	21	87.5
Gm(11)	10	90.9	20	83.3
Gm(21)	7	63.6	8	33.3

The theory of polymorphisms as formulated by Ford⁹ indicates that these multiple forms exist in proportions that cannot be maintained by mutation alone. The theory contends that the different genes are maintained in the population by differential selection. The selective forces which might maintain the serum protein polymorphisms are not known but studies reviewed here suggest the following hypothesis: polymorphic serum proteins influence the host response to certain infective agents. With respect to Gm types, persons who are heterozygous for Gm factors are less likely to encounter Gm types different from their own and therefore are less likely to develop antibodies to Gm types. Such persons when infected with the agent associated with Australia antigen which contains gamma globulin are likely to develop a persistent infection with Au(1) and minimal liver damage. On the other hand, persons who are homozygous for Gm types (that is have fewer Gm types) are more likely to encounter Gm types different from their own and to develop antibodies to them. Such persons, when infected with the agent associated with Au(1), are likely to have a transient infection but one that is associated with more liver damage. Thus, with respect to the hepatitis agent, it might be better for survival to reproductive age to be heterozygous for Gm types. For other agents, advantages may rest with the homozygote. Work currently in progress will test the validity of this hypothesis. These studies have also generated several additional testable hypotheses.

(1) Anti-Au(1) and anti-Gm, or complexes of the same, are associated with each other in other populations. (2) The same (or a similar) agent which leads to the development of anti-Au(1) may lead to the development of anti-Gm in an individual exposed to it either by transfusion or infection. A corollary of this is that the "SNagg" antibodies (agglutinins in normal sera) and "Ragg" antibodies (rheumatoid factor) are due to infection with Australia antigen agent, or an agent similar to it. (3) Australia antigen, anti-Au(1) and their complexes are related to the pathogenesis of rheumatoid arthritis and related illnesses. These hypotheses are now being tested.

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- ¹ Blumberg, B. S., Sutnick, A. I., London, W. T., and Millman, I., *New Engl. J. Med.*, **283**, 349 (1970).
- ² Blumberg, B. S., *Bull. NY Acad. Med.*, **40**, 377 (1964).
- ³ Blumberg, B. S., Millman, I., Sutnick, A. I., and London, W. T., *J. Exp. Med.*, **134**, 320 (1971).
- ⁴ Vierucci, A., Blumberg, B. S., Dettori, M., Borgotti, L., and Levene, C., *J. Pediatr.*, **72**, 776 (1968).
- ⁵ Vierucci, A., Raggazzini, F., Borgatta, L., London, W. T., Sutnick, A., and Blumberg, B., *Clin. Res.*, **19**, 434 (1971).
- ⁶ Ropartz, C., Rousseau, P.-Y., and Rivat, L., *Rev. Franc. Etud. Clin. Biol.*, **6**, 591 (1961).
- ⁷ Blumberg, B. S., and Riddell, Nancy M., *J. Clin. Invest.*, **42**, 867 (1963).
- ⁸ Millman, I., Huhtanen, Hanna, Merino, F., Bayer, M. E., and Blumberg, B. S., *Res. Commun. Chem. Pathol. Pharmacol.*, **2**, 667 (1971).
- ⁹ Ford, E. B., *Genetic Polymorphisms* (Faber and Faber, London, 1965).

Evidence for Linkage between Human Loci for 6-Phosphogluconate Dehydrogenase and Phosphoglucomutase₁ in Man-Chinese Hamster Somatic Cell Hybrids

THE existence of zymographically detectable interspecific enzyme variations and the preferential loss of human chromosomes in the man-mouse as well as the man-Chinese hamster somatic cell hybrids have rendered these hybrids useful for genetic analysis of man^{1,2}. Of these two systems, linkage studies involving the human locus for 6-phosphogluconate dehydrogenase, *6PGD*, have been found feasible only in the

	PGM ₁		IPO A		6PGD		LDH B	
	+	-	+	-	+	-	+	-
LDH A	+33	21	33	21	33	00	43	11
	-00	46	21	25	21	46	35	11
	28/83		28/83		28/83		28/83	
LDH B	+25	54	46	33	25	54		
	-07	14	07	14	07	14		
	28/83		28/83		28/83			
6PGD	+37	00	25	07				
	-00	63	29	39				
	67/83		28/83					
IPO A	+25	29						
	-07	39						
	28/83							

Fig. 1 Linkage relationships between five well known human autosomal enzyme markers segregating in man-Chinese hamster somatic cell hybrids. The data presented in Table 1 have been broken down according to 2 × 2 format following the general methodology suggested by Ruddle *et al.*¹⁰ and tabulated in +/+, +/-, -/+, -/- possible categories for particular pairs of markers. The results are given in percentages. Note that the fraction of the total number of clones from which the data were obtained for each of the marker pair combinations is also indicated.

man-Chinese hamster hybrids because the usual phenotype of human *6PGD* is electrophoretically distinguishable only in this hybrid system³. This report deals with the genetic linkage relations of the human *6PGD* locus in man-Chinese hamster somatic cell hybrids and provides the first evidence that the human genes for *6PGD* and phosphoglucomutase₁ (*PGM*₁) are syntenic (located on the same chromosome)⁴.

The hybrid cell lines a3/MS2, a23/MS2 I and a23/MS2 II were derived from two different thymidine kinase (TK) deficient Chinese hamster cell lines (a3 and a23) and a male human fibroblastic cell strain, MS2, deficient in hypoxanthine-guanine phosphoribosyl transferase (HGPRT); Wg3-h/lymph series were produced by a fusion between HGPRT deficient Chinese hamster cells (Wg3-h) and phytohaemagglutinin-stimulated human lymphocytes. The details on production, isolation and propagation of these hybrid cell lines, including clones and their subclones, were described earlier^{2,5}.

The electrophoretic phenotypes of various hybrid cell lines, using appropriate parental cell lines and strains as controls, were determined as before³, on cellulose acetate gel, for the following enzymes: lactate dehydrogenases (LDH A and

Fig. 2 Zymograms of *6PGD* (top) and *PGM*₁ (bottom) comparing the (1) Chinese hamster, (2) human, (3) artificial mixture of Chinese hamster and human, and (4-9) man-Chinese hamster somatic cell hybrid patterns. The human fibroblastic cell strain (channels 2 and 3) was derived from a donor with the *PGM*₁ 2-1 phenotype but with the usual *6PGD*. The human partners in this hybrid series, however, were derived from donors with usual phenotypes, *PGM*₁ 1 and *6PGD* A. The intermediate band due to heteropolymeric enzyme molecules seen in *6PGD* (channels 4-7) is absent in *PGM*₁³. Nevertheless, their relative intensities can be compared (see text). The last two hybrids (channels 8 and 9) have lost the two human loci.



Table 1 Segregation of Human Enzyme Markers in Eighty-three Clonal and Subclonal Populations of Man-Chinese Hamster Somatic Cell Hybrids

Hybrid cell line	No. of clones	HGPRT	G6PD	PGK	LDH A	LDH B	PGM ₁	6PGD	IPO A	IDH	MDH
a3/MS2 I	6	—	+	+	+	+	+	+	+	—	—
	1	—	—	—	—	+	—	—	—	—	—
	1	—	—	—	+	—	—	—	+	—	—
	1	—	—	—	+	+	—	—	—	—	—
	1	—	+	+	+	+	—	—	+	—	—
	1	—	+	+	+	+	—	—	—	—	—
	1	—	—	—	+	+	+	+	+	—	—
	12	—	+	+	—	—	+	+	—	—	—
	2	—	+	+	—	—	—	—	—	—	—
	2	—	—	—	—	—	+	+	—	—	—
a23/MS2 I	5	—	+	+	—	+	—	—	+	—	—
	1	—	—	—	+	+	—	—	—	—	—
	4	—	+	+	—	—	—	—	—	—	—
	1	—	+	+	—	—	—	—	+	—	—
a23/MS2 II	4	—	—	—	—	+	—	—	—	—	—
	1	—	—	—	+	+	—	—	—	—	—
Wg3-h/lymph I	1	+	+	+	+	—	+	+	—	—	—
	2	+	+	+	—	—	+	+	—	—	—
	2	+	+	+	—	—	—	—	—	—	—
	33	+	+	+	—	—	—	—	—	—	—
	1	—	—	—	+	—	+	+	—	—	—

Blank, not tested; (—), no enzyme activity; (+), activity present. No attempt is made to indicate the relative intensities of various enzyme activity bands which appeared on the zymograms.

LDH B), NAD-dependent cytoplasmic malate dehydrogenase (NAD-Cyto-MDH), NADP-dependent cytoplasmic isocitrate dehydrogenase (NADP-Cyto-IDH), phosphoglucomutase₁ (PGM₁), 6-phosphogluconate dehydrogenase (6PGD)⁶, indophenol oxidase A (IPO A)⁷, glucose-6-phosphate dehydrogenase (G6PD)⁸, hypoxanthine-guanine phosphoribosyl transferase (HGPRT)⁹ and phosphoglycerate kinase (PGK): their homologous forms in man and Chinese hamster are distinguishable on zymograms, with the exception of LDH B (ref. 3).

The data obtained from eighty-three hybrid clones and subclones are summarized in Table 1. A large fraction of these lines (sixty-six) had already been used to confirm the X-linkage of PGK using the human G6PD and HGPRT as main markers⁵. Using the same criterion we concluded that the other markers listed in Table 1 are autosomal in man. The human markers NAD-Cyto-MDH and NADP-Cyto-IDH were lost in all the clones, indicating that these two loci are not linked to the other loci: earlier studies^{3,10} suggested that these two loci are asyntenic (not present on the same chromosome) in man. Only data pertaining to the rest of the five markers, therefore, are included for further analysis in Fig. 1, in which the only pair that apparently exhibits absolute linkage is PGM₁ and 6PGD. Of the four lines listed in Table 1, only a3/MS2 I and Wg3-h/lymph I cell hybrids seem to be informative for further linkage analysis involving human 6PGD, for the other two lines have lost the human 6PGD activity in all their clones and subclones tested. Only data obtained from the clones and subclones derived from the former, therefore, are included in Fig. 1 for the 6PGD-PGM₁ pair: 37% of them have retained the human loci for 6PGD and PGM₁ together while the rest have lost them together; there was no instance of dissociation in sixty-seven opportunities.

Because the loss of human chromosomes in these hybrid cells seems to be progressive, the expressions of linked loci for constitutive enzymes should maintain reflective proportions in any heterogeneous group of hybrid "clones"⁵. The zymogram patterns of 6PGD and PGM₁ are seen in Fig. 2. The relative intensities of human 6PGD compared with those of human PGM₁ among different hybrid cell lines (channels four to nine) are strikingly reflective (which is not the case between the other possible pairings of these five enzymes). This finding is a further suggestion for linkage between the two loci in question. Nevertheless, non-randomness in the loss of certain groups of human chromosomes, which was

encountered in man-mouse hybrids¹¹ as a possible cause of spurious linkages, cannot be excluded at this stage². It is, therefore, imperative to wait for a suitable selectable biochemical marker ascribable to the putative human autosome carrying the 6PGD locus, in order to confirm this linkage using somatic cell hybrids^{5,11,12}.

Human family studies indicate that the loci for 6PGD and PGM₁ are not within measurable distance^{13,14}, but this finding need not necessarily eliminate the possibility that the two loci are located on the same chromosome. Pedigree studies by Weitkamp *et al.*¹⁴ have revealed that the 6PGD is linked to Rh (the rhesus set of blood group loci). It was known that one of the loci for elliptocytosis, El₁, is closely linked to Rh in man¹⁵. On the basis of data obtained from fifty-one pedigrees, Renwick¹⁶ has estimated the Rh : PGM₁ interval to be 0.27 Morgans and reasoned that Rh and El₁ lie between PGM₁ and 6PGD. He has thus shown that "the study of pedigrees and the study of cell hybrids could complement each other in a gratifying manner" for the mapping of human autosomes¹⁶.

Studies on man-mouse somatic cell hybrids indicate that the human PGM₁ is on a C group chromosome¹⁷ and an analysis of data collected from a human pedigree with a variant chromosome 9 suggested linkage of Rh to the C₉ (ref. 18). Studies are in progress on the specific identification of individual human chromosomes^{19,20} in this series of man-Chinese hamster hybrids in order to confirm the localization of 6PGD: Rh-El₁ : PGM₁ quartet¹⁶ on the human C₉.

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- ¹ Weiss, M. C., and Green, H., *Proc. US Nat. Acad. Sci.*, **58**, 1104 (1967).
- ² Westerveld, A., Meera Khan, P., Visser, R. P. L. S., and Bootsma, D., *Nature New Biology*, **234**, 20 (1971).
- ³ Meera Khan, P., *Arch. Biochem. Biophys.*, **145**, 470 (1971).
- ⁴ Meera Khan, P., and Westerveld, A., *Fourth Intern. Cong. Hum. Genet.*, Paris (abstr.) (1971).
- ⁵ Meera Khan, P., Westerveld, A., Grzeschik, K.-H., Deys, B. F., Garson, O. M., and Siniscalco, M., *Amer. J. Hum. Genet.* (in the press).
- ⁶ Meera Khan, P., and Rattazzi, M. C., *Biochem. Genet.*, **2**, 231 (1968).
- ⁷ Brewer, G. J., *Amer. J. Hum. Genet.*, **19**, 674 (1967).
- ⁸ Rattazzi, M. C., Bernini, L. F., Fiorelli, G., and Mannucci, P. M., *Nature*, **213**, 79 (1967).
- ⁹ Shin, S., Meera Khan, P., and Cook, P. R., *Biochem. Genet.*, **5**, 91 (1971).
- ¹⁰ Ruddle, F. H., Chapman, V. M., Ricciuti, F., Murnane, M., Klebe, R., and Meera Khan, P., *Nature New Biology*, **232**, 69 (1971).
- ¹¹ Nabholz, M., Miggiano, V., and Bodmer, W., *Nature*, **223**, 358 (1969).
- ¹² Migeon, B. R., and Miller, C. S., *Science*, **162**, 1005 (1968).
- ¹³ Edwards, J. H., and Wingham, J., *Ann. Hum. Genet.*, **30**, 233 (1967).
- ¹⁴ Weitkamp, L. R., Guttormsen, S. A., Shreffler, D. C., Sing, C. F., and Napier, J. A., *Amer. J. Hum. Genet.*, **22**, 216 (1970).
- ¹⁵ Lawler, S. D., *Caryologia*, Supplement, **6**, 26 (1954).
- ¹⁶ Renwick, J., *Nature*, **234**, 475 (1971).
- ¹⁷ Conover, J. H., and Hirschhorn, K., *Amer. Soc. Hum. Genet.*, Meeting, Abstr., **23**, San Francisco (1969).
- ¹⁸ Palmer, C. G., and Schroder, J., *J. Med. Genet.*, **8**, 202 (1971).
- ¹⁹ Caspersen, T., Zech, L., and Johansson, C., *Exp. Cell Res.*, **62**, 490 (1970).
- ²⁰ Miller, O. J., Allderice, P. W., Miller, D. A., Berg, W. R., and Migeon, B. R., *Science*, **173**, 244 (1971).

Molecular Mechanism of Tay-Sachs Disease

TAY-SACHS disease is an inherited disorder of the central nervous system which becomes clinically evident in the fourth to sixth month of life, is characterized by progressive neurological impairment, and leads to death usually before the age of 4. The development of pathological changes in the brain is associated with the accumulation of excess GM₂* ganglioside¹. The gangliosides are a class of sialic acid-containing glycosphingolipids normally found at highest concentration in the ganglion-cell-rich fraction of the brain. GM₂ is a monosialo form present in only minute quantities in normal brain.

Speculation about the pathogenesis of the cytological changes associated with GM₂ ganglioside accumulation centres on two possibilities. The observed changes may be due to stereospecific characteristics of the GM₂ head-group, or, alternatively, to less specific physicochemical properties of the general class of gangliosides. The existence of a similar disease associated with excess accumulation of GM₁ ganglioside favours the second hypothesis. Nevertheless, there have been surprisingly few attempts to relate the physico-chemical properties of gangliosides to the Tay-Sachs disease mechanism. Mixed ox brain gangliosides form micelles in aqueous solution, and the size and shape of these aggregates have been characterized². Mixed micelles are formed from aqueous dispersions of gangliosides and lysolecithin², and gangliosides complex with certain cationic dyes³. Mixtures of ganglioside, and other cellular constituents in chloroform, form bodies with the appearance of Tay-Sachs membranous cytoplasmic bodies (MCB) when dried, sectioned, and prepared for ultramicroscopic examination⁴.

* GM₂ is the nomenclature adopted by Svennerholm⁸ for (N - [1 - 4] - [[O - 2 - acetamido - 2 - deoxy - β - D-galactopyranosyl] - (1→4) - O - [N - acetyl - neuraminyl - (2→3)] - O - β - D-galactopyranosyl] - (1→4) - β - D - glucopyranosyl]oxy)methyl] - 2 - hydroxy - 3 - heineicosenyl] octadecanamide), Tay-Sachs ganglioside.

We have, therefore, begun to examine the molecular mechanisms underlying Tay-Sachs cytopathology, using the interactions of gangliosides with phosphatidyl choline (lecithin) as a model of ganglioside-lipid interactions. Purified mixed beef brain gangliosides were prepared by established techniques⁵, and purified egg lecithin was prepared by column chromatography. The interaction between gangliosides and lecithin was studied qualitatively by examining "myelins" formed by the hydration of dried lipid films under crossed Nicol prisms. "Myelins" formed from ganglioside-lecithin mixtures showed wide lamellar spacings when compared with those formed from lecithin alone. The widened spacing was thought to be introduced by the intercalation of ganglioside molecules with charged head-groups in the lamellae of the smectic mesophase. The association of the two molecules was quantified by taking chloroform-methanol solutions of mixed gangliosides plus lecithin and combining them in proportions varying from 0-100% of each substituent. These were dried *in vacuo* and redissolved in an aqueous solution containing 9 mM KCl, 1 mM histidine buffer (pH 6.5). Final total concentrations of lipid equalled 1 to 2 mM, and mixtures with 0-20% ganglioside were restudied at total lipid concentrations of 10-25 mM in order to increase sensitivity. The mixtures were equilibrated under N₂ at 22° C for 24 h and then centrifuged for 30 min at 100,000g. The concentrations of ganglioside and phospholipid were determined in the initial lipid swell, the supernatant, and the pellet.

The results showed that at relative concentrations of ganglioside $\left(\frac{\text{ganglioside (mol)}}{\text{ganglioside (mol)} + \text{lecithin (mol)}} \times 100 \right)$ less than

30%, more than 95% of the total lipid sedimented, and the pellet was in the form of a smectic mesophase. At relative concentrations of ganglioside more than 65%, the bulk of the lecithin was in the supernatant, although as the relative concentration of lecithin approached 65% a top to bottom lipid concentration gradient was present in the clear solution contained in the centrifuge tube. At these proportions the lecithin presumably was held in mixed ganglioside-lecithin micelles, the increasing degree of sedimentation suggesting an enlargement or alteration of micellar shape as the proportion of lecithin was increased. At relative concentrations of ganglioside between 30 and 65%, both a clear lipid-containing supernatant (43 to 57% ganglioside) and a pellet (35 to 49% ganglioside) were observed. Ganglioside-lecithin mixtures containing relative ganglioside concentrations of 45 to 48% formed a metastable, homogeneous, clear, viscous phase which resolved into pellet and supernatant on standing for 48 h.

It is suggested that the lamellar MCB, which are composed of 20 to 50% ganglioside mixed with cholesterol, phospholipid, and protein, and which fill the cytoplasm of ganglion cells in Tay-Sachs disease¹, form by similar associative processes to those yielding the lamellar liquid crystalline pellet in synthetic mixtures of ganglioside-lecithin containing 0 to 65% ganglioside. The deposition of lipid in MCB might limit the lipid available for cellular membrane synthesis. The results further suggest that at concentrations of ganglioside above 30% the formation of membranous structures would be inhibited by lipid micellization. Provided that the model reflects conditions *in vivo*, and that sufficiently high localized concentrations of unbound ganglioside are reached, an explanation is provided for the failure of myelin synthesis postulated to occur in some individuals with Tay-Sachs disease.

On the other hand, it is often observed that ganglion cell organelles remain well preserved, in spite of high intracellular ganglioside concentrations, until late in the course of the disease. Similarly, formed myelin maintains its structure until advanced axonal disintegration leads to Wallerian demyelination⁶. While the preservation of these structures may result from ganglioside binding, the observations are compatible with studies in which gangliosides and lecithin were hydrated separately and the aqueous solutions were then

combined. In these studies, therefore, the entry of gangliosides into preformed lecithin "myelins" was observed. After incubation for 24 h, centrifugation, and assay, more than four fifths of the ganglioside was found in the supernatant, even in mixtures of ganglioside-lecithin containing relative ganglioside concentrations of as little as 15%. Equally, there was no measurable lecithin in the supernatant at relative concentrations of ganglioside up to 100%. It thus seems that preformed lecithin "myelins" resist solubilization by gangliosides, and that only the outer monolayer of the "myelins" absorbs gangliosides in the conditions of study. It is suggested that entry of ganglioside monomers into the interior of the preformed lecithin "myelins" was retarded by the high energetic requirements for movement of the bulky, hydroxylated and charged, hydrated head-groups across a lipid bilayer. A similar hydration barrier has been reported in studies of the solubilization of methyl linoleate by ceto-macrogol⁷. The resistance of formed ganglion cell membranes and myelin to dissolution by high concentrations of ganglioside may thus result from a low rate of penetration. Although the structure of the membrane involved differs, it is perhaps noteworthy that there was no evidence of haemolysis when washed human red cells were suspended in 0.15 M NaCl aqueous solutions containing mixed gangliosides at ten times the critical micellar concentration.

While alternative mechanisms are possible, the experimental results provide a sufficient explanation for the principal histological findings in Tay-Sachs disease. It is proposed to publish a more detailed account of this work, and of further studies of ganglioside-lecithin interactions, at a later date.

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- ¹ Fredrickson, D. S., and Trams, E. G., in *The Metabolic Basis of Inherited Disease* (edit. by Stanbury, J. B., Wyngaarden, J. B., and Fredrickson, D. S.) (McGraw-Hill, New York and London, 1966).
- ² Gammack, D. B., *Biochem. J.*, **88**, 373 (1963).
- ³ Albers, R. W., and Koval, G. J., *Biochim. Biophys. Acta*, **60**, 359 (1962).
- ⁴ Samuels, S., Gonatas, N., and Weiss, M., *J. Neuropathol. Exp. Neurol.*, **24**, 256 (1965).
- ⁵ Penick, R. J., Meisler, M. H., and McCluer, R. H., *Biochim. Biophys. Acta*, **116**, 279 (1966).
- ⁶ Terry, R. D., and Weiss, M., *J. Neuropathol. Exp. Neurol.*, **22**, 18 (1963).
- ⁷ Carless, J. E., and Nixon, J. R., *J. Pharm. Pharmacol.*, **12**, 348 (1960).
- ⁸ Svennerholm, L., *J. Neurochem.*, **10**, 613 (1963).

Knuckle Walking Hand Postures in an Orangutan (*Pongo pygmaeus*)

AN obese 16 yr old male orangutan, named Felix, at the Chicago Zoological Park, Brookfield, Illinois, consistently places his hands in knuckle walking postures while sitting-resting (Fig. 1), sitting-feeding and engaging in a distinctive mode of squatting bipedal progression.

During sitting-feeding and sitting-resting, one or both hands are characteristically placed directly in front of the body.

The fingers are flexed so that the dorsal skin on the middle phalanges of digits II-IV or II-V is the principal manual contact with the substrate. The proximal phalanges of manual digits II-V are approximately aligned with metacarpals II-V or they may be abducted slightly (Fig. 1). There is negligible or very slight hyperextension of metacarpophalangeal joints II-V. The wrist joints show notable ulnar deviation (adduction) and the elbow joints are flexed. Digits III and IV seem to bear the major portion of weight in the resting forelimb.



Fig. 1 Felix, an adult male orangutan, sitting-resting with knuckle walking postures of both hands and both hindlimbs tucked beneath his abdomen.

Felix often squats in a bipedal posture when moving slowly forwards or sideways on the floor. The thighs are markedly flexed, abducted and rotated laterally so that they are tucked under and often against his ponderous abdomen. The knees are sharply flexed. The feet are supinated remarkably so that only their lateral aspects contact the floor. Pedal digits II-V are held flexed and the halluces do not touch the floor. The back is maintained in a rigid, fully erect posture. Most of the load seems to be borne by the feet and ischial tuberosities.

Each hindlimb step is accomplished by leaning sideways and slightly forwards onto one foot and haunch so that the other foot may be elevated a few inches and swung free of the ground. The hand ipsilateral with the swinging foot is concurrently swung forwards though their releases and contacts are not precisely coincident. The contralateral hand rests in a knuckle walking posture in front of the supporting foot. It generally does not bear much weight in excess of the forelimb itself. As the load shifts onto the supporting foot and haunch the elbow and wrist of the knuckle walking hand flex and adduct instead of bracing to support part of the load.

Further observations suggest that the forelimbs are not essential load-bearing supports during squatting bipedalism. Felix waddles forwards without interrupting his pace while

picking up and holding food in one free hand. He also waddles forwards with one or both hands touching overhanging objects but not providing suspensory support for the body. He sometimes moves over short distances with both forelimbs raised and outstretched above his head.

When waddling on a wet floor, he slides his knuckle walking hands in front and without breaking contact with the substrate. As one foot swings forwards, the load is borne almost exclusively on the contralateral foot and haunch.

When moving rapidly on a dry substrate, he raises into a semi-erect quadrupedal position. He places his hands in fist walking postures wherein the fingers are tightly flexed and the skin on the dorsum of proximal phalanges II-V makes contact with the substrate. The hindlimbs are extended and the ischial tuberosities are well above the substrate. The back and head are inclined forwards. The load is borne not only on the lateral aspects of the feet but also on the fists as the subject uses a "diagonal-sequence, diagonal couplets gait"¹.

He moves rapidly on a wet floor with alternate steps of the hindlimbs but without raising his fists from the substrate. Once he briefly slid his right hand forwards in a knuckle walking posture while his left hand remained a fist. The right hand bore only a moderate portion of the load because the forelimbs remained protracted throughout the episode and the body did not pass over the hands.

When leaning forwards to investigate or to pick up orally objects on the floor and when descending head first from low elevations, he consistently places his hands in fist walking postures.

In summary, although Felix often places his hands in knuckle walking postures, he rarely supports a major portion of his body weight on knuckle walking hands. Instead, he places his hands in fist walking postures when support is required for loads that are significantly greater than the weight of the forelimbs themselves. By fist walking he probably avoids stressing metacarpophalangeal joints II-V which, in orangutans, lack special morphological adaptations for knuckle walking of the kind possessed by gorillas and chimpanzees²⁻⁴.

Before 1967, the primatological and anthropological literature was confusing and misleading about the terrestrial hand postures of great apes because some authorities uncritically and sometimes erroneously designated orangutans, as well as chimpanzees and gorillas, "knuckle walkers"⁵.

One of us (R.T.) recently described and classified⁶ the variety of hand postures often used by captive orangutans during terrestrial locomotion, and concluded that only chimpanzees and gorillas should be designated knuckle walkers. He stated that "orangutans do not and, moreover, cannot assume the digitigrade hand posture of the African apes"⁶. This statement should now be qualified and restricted to comparisons between great apes engaged in semi-erect quadrupedal progression with "trot" and "diagonal sequence, diagonal couplets" gaits¹ on non-lubricated substrates. Although Felix has not been observed to knuckle walk like an African ape or to place his hands in knuckle walking postures during "crutch walking" as do chimpanzees and gorillas, he frequently rests his hands on the middle segments of the fingers and thereby supports on them the weight of his forelimbs and perhaps also a portion of his head and upper torso weight.

Because a highly advanced arboreal climber and arm swinger like an orangutan is able to place his hands in knuckle walking postures suggests that the ancestors of the African apes might have been similarly, or to a greater extent, predisposed to knuckle walking by their own special arboreal heritage.

Man, too, often rests his flexed fingers in facultative knuckle walking postures, as may be witnessed in certain public speakers and football linemen. Although the thumb is usually used prominently as a supporting strut during human knuckle walking postures, the fact that man has a predisposition for such placement of manual digits II-V may be at least as provocative for evolutionary inferences as the facultative knuckle walking of an orangutan.

It may thus be argued that man passed through a phase of arboreal climbing and suspensory posturing somewhat more advanced than the antibrachiationists and prebrachiationists have admitted into their models^{3,7}. Another optional model would evolve man, orangutans, or both from knuckle walking ancestors. Such a theoretical possibility cannot be ruled out on the basis of available evidence but we do not choose to subscribe to it.

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¹ Hildebrand, M., *Amer. J. Phys. Anthropol.*, **26**, 119 (1967).

² Tuttle, R. H., *Amer. J. Phys. Anthropol.*, **26**, 171 (1967).

³ Tuttle, R. H., *Science*, **166**, 953 (1969).

⁴ Tuttle, R. H., in *The Chimpanzee* (edit. by Bourne, G. H.), **2**, 167 (Karger, Basle/New York, 1970).

⁵ Straus, W. L., *Amer. J. Phys. Anthropol.*, **27**, 199 (1940).

⁶ Tuttle, R. H., *Amer. J. Phys. Anthropol.*, **26**, 171 (1967).

⁷ Tuttle, R. H., *Sci. J.*, **5A**, No. 5, 66 (1969).

Interpretation of Persistence and Effects of Polychlorinated Biphenyls in Birds

Peakall and Lincer¹ suggest that polychlorinated biphenyls (PCBs) found in nature are derived only from highly chlorinated commercial mixtures such as 'Aroclor 1254'. Residues of lower chlorinated mixtures have not been reported in spite of their predominant industrial use. This may be due either to utilization in enclosed systems or to more rapid metabolism or excretion. To demonstrate which residues remain after PCB feeding, pigeons (*Columbia livia*) and Japanese quail (*Coturnix coturnix japonica*) have been fed 'Aroclor' mixtures.

Twenty-four separately caged feral pigeons were fed *ad libitum* for 28 days with wheat dressed with 500 p.p.m. 'Aroclor 1242'. Six control pigeons were fed wheat. At the end of the feeding period six test birds were killed by cervical dislocation and the remainder returned to a diet of mixed grain and pulses, before being killed in batches of six at 28, 56 and 168 days. Eighteen 4 week old female Japanese quail were caged in batches of six. One batch was fed *ad libitum* for 20 days with 'Aroclor 1242' dressed food at 250 p.p.m., another with 'Aroclor 1254' dressed food at 250 p.p.m. and the remaining batch left as controls. All birds were killed 24 h after withdrawal of dressed food. This regimen allows comparison with other quail feeding experiments². Immediately after death, breast muscle, liver, brain and omental fat samples were removed from pigeons. Similar samples were removed from quail with the substitution of heart for breast muscle. A

Table 1 Mean Total PCB Residues (p.p.m.), found in Quail Tissue after Feeding 'Aroclor 1242' and 'Aroclor 1254' at 250 p.p.m. for 20 Days

Tissue	'Aroclor 1242'	'Aroclor 1254'
Liver	17.0 ± 2.6 *	28.1 ± 7.9
Heart	3.2 ± 0.7	7.0 ± 1.1
Brain	7.8 ± 1.7	7.7 ± 2.3
Omental fat	123 ± 17	304 ± 31

* All figures are mean of six birds ± s.e.

portion of liver was taken for preparation of microsomes² and determination of cytochrome P₄₅₀³ and microsomal protein⁴. The remaining liver and the other tissues were extracted by the method of Taylor *et al.*⁵ before gas-liquid chromatographic analysis using a 3-foot 'Apiezon L' column⁶ at 200° C.

The complex nature of 'Aroclor' mixtures makes the expression of results difficult. Because gross changes have taken place in our experiment we have chosen the method of Risebrough⁷ from those published and compared the sum total of peak heights with a 1,1-di(4-chlorophenyl)-2,2-dichloroethylene (DDE) standard, which in turn was related to a known weight of 'Aroclor 1242'. The mean results obtained from the batches of pigeons are shown in Fig. 1 and from quail in Table 1. Regular checks made on excreta revealed no gross excretion of unchanged material.

The presentation of changes in the gas-liquid chromatographic pattern of PCB isomers is also difficult. Most workers have preferred to suggest that the patterns which they have obtained resemble one of the commercial mixtures, leading to the general conclusion that PCBs remain unaltered in the biosphere. Since we wished to determine whether birds are able to metabolize PCBs we adopted the following method of presentation for gas-liquid chromatographic data. A single peak occurring in all chromatograms from fed birds was selected and represented arbitrarily as 100 units. The mean of peak height for each relative retention time from each batch of birds was normalized to this peak. By this method an average residue "spectrum" can be presented in the form of a

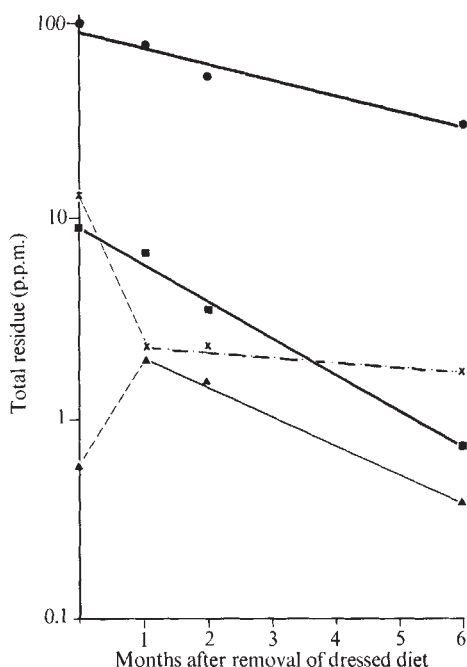


Fig. 1 Mean total levels of PCB in pigeon tissues following feeding of 'Aroclor 1242' at 500 p.p.m. in diet for 28 days. ●, Fat; ×, liver; ■, muscle; ▲, brain.

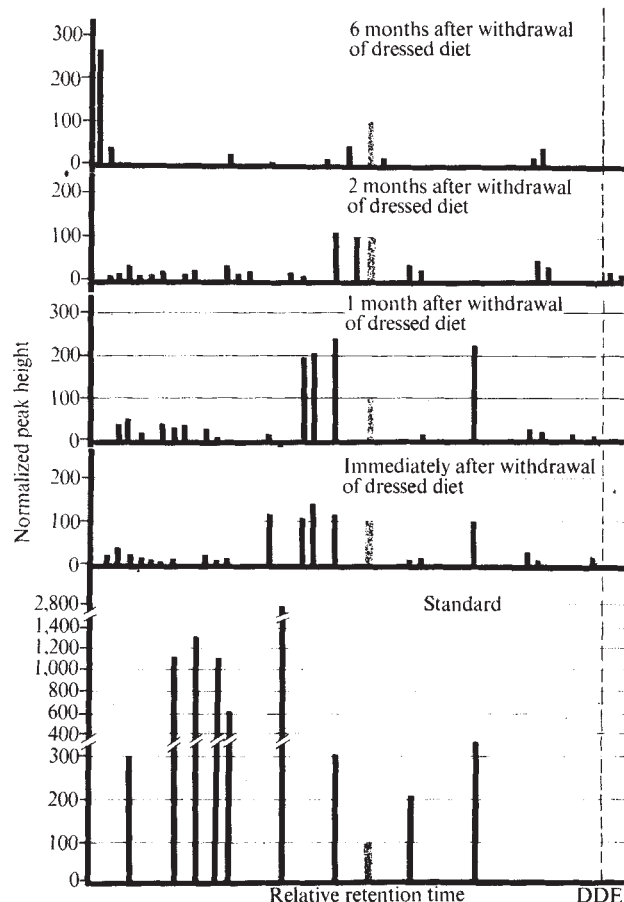


Fig. 2 Gas-liquid chromatographic "spectra", normalized to a common peak (stippled column) of 'Aroclor 1242' standard and mean pigeon liver residues following feeding at 500 p.p.m. in diet for 28 days.

line diagram. Fig. 2 shows line diagrams from the livers of pigeons fed 'Aroclor 1242', and Fig. 3 those from quail fed 'Aroclor 1254'. Other tissues gave similar results.

Total PCB residues immediately after withdrawal of treated food show a similar distribution between tissues to those in pigeons fed 1,1-di(4-chlorophenyl)-2,2,2-trichloroethane (DDT)⁸. Allowing for the higher feeding level in the DDT study initial PCB residues are five to ten times higher. In the muscle and fat there is a steady logarithmic decay with half-lives, by inspection, of 50 days and 125 days respectively. After an initial large drop in levels the liver residues also follow a logarithmic decay with a half-life of 140 days. These figures compare⁸ with a statistically computed half-life of 28 days for DDT in all pigeon tissues (uncertainty in interpreting PCB analytical results precludes statistical analysis). PCB residues in the brain reach a maximum and then decay logarithmically with a half-life of 50 days. The high liver residue level immediately after withdrawal of food may be attributable to the rate at which liver receives freshly absorbed PCB, and the initial low brain level may reflect the operation of the blood-brain barrier⁹.

Total residues in quail fed 'Aroclor 1242' (Table 1) are higher than those in pigeons in spite of a shorter feeding period at half the level. Food consumption per unit weight of quail, however, is two to three-fold larger than that of pigeons. Residues of 'Aroclor 1254' are generally twice those of 'Aroclor 1242', suggesting that this mixture is more difficult to metabolize or excrete.

The standard 1242 mixture gives a pattern dominated by a few isomers of low retention time on our gas-liquid chromatograph. There is a considerable change in pigeon liver residue patterns (Fig. 2) with peaks of low relative retention times considerably reduced immediately following withdrawal of

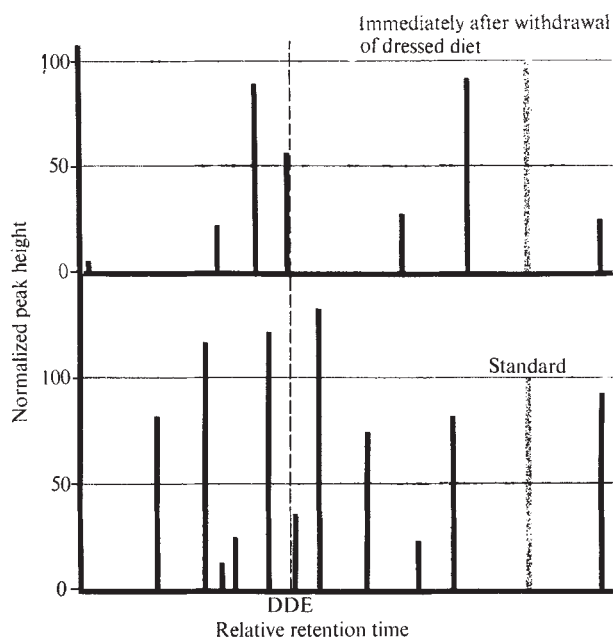


Fig. 3 Gas-liquid chromatographic "spectra", normalized to a common peak (stippled column) of 'Aroclor 1254' standard and mean quail liver residues following feeding at 250 p.p.m. for 20 days.

treated food and virtually absent by the end of the experiment. These peaks seem to be readily removed from the body revealing other minor or less electron capturing constituents with a longer biological half-life. We cannot yet be certain that all these peaks are chlorinated biphenyls present in the original mixture; some may be metabolites. Peaks with a higher retention time are relatively enhanced over the experimental period. The patterns obtained after feeding quail 'Aroclor 1242' have the same general features but 'Aroclor 1254' feeding produces less aberration from the standard.

The conclusion that the less chlorinated isomers are more readily metabolized is also supported by two analyses on a high resolution capillary column. A standard 'Aroclor 1242' exhibited forty-four peaks and a considerable proportion could be assigned structures¹⁰. An extract of fat from a pigeon killed immediately after withdrawal of dressed food exhibited twenty-nine peaks. Most of the fifteen peaks of lowest retention time (mainly dichloro and trichloro isomers) were absent from the extract. Peaks of longer retention time (mainly tetrachloro or higher chlorinated isomers) were present in the pigeon and many were relatively enhanced. These results agree with previous work involving quail¹¹ and rats¹².

The hepatic microsomal systems responsible for metabolizing foreign compounds are sensitive to induction by chlorinated hydrocarbons. The significance of induction is not yet understood but it can be used as an indicator of the biological activity of a compound. Increases in microsomal protein and cytochrome P₄₅₀ are central to microsomal induction and we have measured these to indicate the interference by PCB residues in the normal physiology of the birds (Tables 2 and 3).

Pigeon liver weights remain elevated for at least two months following withdrawal although hepatic microsomal protein returns to normal. In contrast, cytochrome P₄₅₀ levels are still at three times the control level 6 months after returning to normal diet when PCB levels are approximately 2 p.p.m. and composed mainly of higher chlorinated isomers, suggesting that extremely low levels (<1 p.p.m.) of these isomers cause significant elevation of microsomal enzymes. Quail fed either 'Aroclor 1242' or '1254' show similar increases which are far larger than those obtained from similar experiments involving DDT and DDE. 'Aroclor 1254' produces considerably more

Table 2 Mean Liver Weights, Microsomal Protein Levels, Cytochrome P₄₅₀ Levels and Residue Levels for Pigeons fed 'Aroclor 1242' at 500 p.p.m. for 28 Days and Killed at 0, 28, 56 and 168 Days after the Withdrawal of Dressed Food

Days to death	Mean liver weight (g)	Microsomal protein mg g ⁻¹ liver	Cytochrome P ₄₅₀ nmol g ⁻¹ liver	Total liver residues p.p.m.
Control	6.97 ± 0.32 *	13.70 ± 1.07	2.40 ± 0.28	0
0	10.75 ± 0.98	19.30 ± 1.80	15.47 ± 1.70	15.3 ± 1.8
28	8.78 ± 0.61	17.31 ± 1.51	11.00 ± 1.46	3.6 ± 0.5
56	9.74 ± 0.93	13.47 ± 1.72	7.48 ± 0.83	3.4 ± 0.1
168	6.50 ± 0.45	12.81 ± 1.40	6.73 ± 0.81	1.8 ± 0.2

* All figures are mean of six birds ± s.e.

Table 3 Mean Liver Weights, Microsomal Protein Levels, Cytochrome P₄₅₀ Levels and Residue Levels for Quail fed 'Aroclor 1242' and 'Aroclor 1254' at 250 p.p.m. for 20 Days before Death

Compound fed	Mean liver weight (g)	Microsomal protein mg g ⁻¹ liver	Cytochrome P ₄₅₀ nmol g ⁻¹ liver	Total liver residues p.p.m.
Control	3.82 ± 0.22 *	25.05 ± 2.27	5.42 ± 0.64	0
'Aroclor 1242'	4.52 ± 0.37	31.62 ± 1.27	22.18 ± 2.83	17.0 ± 2.6
'Aroclor 1254'	5.08 ± 0.22	42.87 ± 1.42	42.21 ± 3.31	28.1 ± 7.9

* All figures are mean of six birds ± s.e.

induction than '1242', supporting the suggestion above that the more highly chlorinated biphenyls are the most potent inducers.

In spite of analytical and interpretive difficulties we can conclude that pigeons and quail metabolize polychlorinated biphenyls at a rate generally dependent on the amount of chlorine in the molecule. Further work in our laboratory suggests that some lower chlorinated isomers are metabolized extremely rapidly. This could account for the almost universal finding of residues of 'Aroclor 1254' in spite of the major production of '1242'. But biological activity depends on the highly chlorinated isomers, which may need to be taken into account.

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- Peakall, D. B., and Lincer, J. L., *Bioscience*, **20**, 958 (1970).
- Bunyan, P. J., Townsend, M. G., and Taylor, A. (in the press).
- Omura, T., and Sato, R., *J. Biol. Chem.*, **239**, 2370 (1964).
- Lowry, O. H., Rosebrough, N. J., Farr, A. L., and Randall, R. J., *J. Biol. Chem.*, **193**, 265 (1951).
- Taylor, A., Rea, R. E., and Kirby, D. R., *Analyst*, **89**, 497 (1964).
- Simmons, J. H., and Tatton, J. O'G., *J. Chromatog.*, **27**, 253 (1967).
- Risebrough, R. W., in *Chemical Fallout* (edit. by Berg, G. G., and Miller, M. W.), 5 (Charles C. Thomas, Springfield, Illinois, 1969).
- Bailey, S., Bunyan, P. J., Rennison, B. D., and Taylor, A., *Toxicol. Appl. Pharmacol.*, **14**, 13 (1969).
- Bakay, L., *Scientia, Bologna*, **101**, 514 (1966).
- Sissons, D., and Welti, D., *J. Chromatog.*, **60**, 15 (1971).
- Koeman, J. H., Ten Noever De Brauw, M. C., and De Vos, R. H., *Nature*, **221**, 1126 (1969).
- Grant, D. L., Phillips, W. E. J., and Villeneuve, D. C., *Bull. Environ. Contam. Toxicol.*, **6**, 102 (1971).

BOOK REVIEWS

Institutional History

The Archives of the Royal Institution of Great Britain, in Facsimile. Minutes of Managers' Meetings, 1799–1900. Volumes I–II (in one volume), with an introduction by Frank Greenaway. Pp. vii+137+261. (Scolar Press: Menston, Yorks, in association with the Royal Institution, London, 1971.) Set of 15 volumes. £175.

"THE development of the study of the history of science," writes Frank Greenaway in his brief introduction to this volume, "has entailed the raising of standards of critical study, so that the pious hero-worship and chronicle of discoveries which once passed for history of science is far behind us. The historian expects to be disconcerted by his study of sources, and it is a surprise without surprise to find the most recent work completely altering our view of the origin of the Royal Institution, the relation of its founders to each other, the role it played in the community and the influences which bore on the scientific work which it developed."

The managers of the Institution, he says, "were dominated by a large group of landed proprietors keenly interested in the promotion of the technology of agriculture and agricultural products". My discovery of the relations between the governing body at the RI and the Board of Agriculture enabled me to suggest an alternative to the traditional view of the RI, which sees its importance in terms of its leading scientific personalities: Count Rumford, Sir Humphry Davy, and Michael Faraday. We have, I argued, no understanding of the Royal Institution *qua* institution, that is, as a cultural phenomenon. The essential drama of those early years was not (for example) Davy's brilliant experimental work (although that was hardly unimportant), but the role of the RI in the social and economic events of the day, and their impact on it in turn. Dr Greenaway captures this interpretation accurately when he writes that to the managers, "the discoveries we now see as epoch-making were incidents in the maintenance of a state of scientific activity. . . ." It is the institutional context of that scientific activity which I sought to analyse and describe.

If we do wish to integrate the development of science into the context of contemporary events, it will not be enough to consult only the notebooks and published papers of major scientists. Achieving a more synthetic picture necessarily entails the use of institutional archives and records. It is thus a source of great satisfaction to see the documents so carefully preserved in the strong room at the RI finally making their way out into the light of day. If the Royal Institution was indeed as pivotal for the development of modern British science, the publication of the managers' minutes is—and will presumably continue to be—an important contribution to our understanding of the organization of the scientific enterprise in an emerging industrial state.

On first examination, there is little in this volume that seems to be of obvious interest. It contains the weekly comings and goings at 21 Albemarle Street: members added, projects undertaken, apparatus purchased, expenses paid. We learn that philosopher Jeremy Bentham and police magistrate Patrick Colquhoun became life subscribers; that Davy moved into his quarters on March 11, 1801; and that, as an experiment, artisans and mechanics were permitted to attend certain lectures, provided that they confined themselves "to the Gallery only of the Great Lecture Room, and to no other part of the House . . .". A good part of the records deals purely with matters of form, such as the correct order in which the managers' names will be listed in official publications.

Closer examination, however, reveals a situation that takes us far beyond questions of membership, management, or protocol, the managers, as already noted, were among the leading "agricultural improvers" and industrial entrepreneurs of the kingdom. They were men whose conception of science, and interest in its relationship to agriculture and the new sources of wealth, gave them a deep ideological commitment to the institution they had chosen to create. Gradually, a very different picture of the Royal Institution emerges than can be derived from examination of the scientific notebooks alone. The RI was the response of a vigorous aristocracy

to the early changes of the Industrial Revolution; it was a centre of re-orientation of the public purpose of science; it was a way of institutionalizing the economic power that (its founders believed) would accompany the organization of scientific knowledge.

It was no accident, for example, that led the managers to offer the presidency of the Institution to the Duke of Bridgewater as their first choice. The "canal duke", as he was called, was famous for having his engineer, James Brindley, cut a canal between Worsley and Manchester, thereby lowering the transportation costs for his own coal mines. Professor Habakkuk has suggested that for his class, the Duke might well have been "a freak"; but the interest of the managers in having him as their president suggests that he represented an ideal to which they themselves aspired.

The career of Humphry Davy is a more telling illustration of this new entrepreneurial attitude toward science. The instructions to Davy "to absent himself from the Institution during the months of July, August, and September [1801], for the purpose of making himself more intimately acquainted with the practical part of the business of Tanning" (II, 198), were issued at a time when leather manufacture was England's second most important agricultural "industry" (after wool). This "practical chemistry" was not an odd chore performed in exception to Davy's experimental researches; it was his work, part of a rational plan designed by an economically progressive segment of the upper class.

As organized at the Royal Institution, science began to depart from its traditional historical role, as represented, for example, by the Royal Society in the eighteenth century. Polite learning and disinterested research were all well and good, the managers might have agreed; but solving concrete technological problems—such as finding new ways to tan hides—was what science was "really" about. And this Baconian ideal that was flirted with briefly by the Royal Society in the seventeenth century, and only randomly emerging in the form of various provincial clubs at the end of the eighteenth century, was centralized,

institutionalized, and even propagandized by the Royal Institution in the nineteenth century, so much so that it ultimately became the ideological basis on which science grew from modest avocation to full-scale enterprise. The RI was first a challenge, and then a model, for organized scientific research.

A word should be added about the volume itself, which is a handsome one and of obvious quality. The reproduction of the minutes, which was made by photo facsimile, is full folio size and the pages are virtually as clear as those of the original manuscript. A very comprehensive and useful index of all names mentioned in the text has also been provided. Considering the normally high cost of photo reproduction, and the care taken in preparation, the price of the series—£175 for fifteen volumes—would seem to be quite reasonable.

MORRIS BERMAN

Satellites

A Guide to Earth Satellites. Edited by David Fishlock. Pp. xi+159. (Macdonald: London; Elsevier: New York, November 1971.) £2.50.

IN the past two decades few areas of scientific and technological endeavour have commanded such world-wide attention as man's activities in space.

On October 4, 1957, the first small sputnik was triumphantly placed in orbit. In the fourteen years which have elapsed since that historic event, several hundreds of space vehicles of one sort or another have followed Sputnik I into Earth orbit and satellites have become an accepted part of the modern scene. The publication of what can be described as an intelligent man's guide to Earth satellites is then greatly to be welcomed. This volume consists of some eight chapters contributed by authorities in their respective fields. The topics covered include launching vehicles, satellites for communication, meteorology, the study of Earth resources, navigation, scientific research and satellites for military purposes. The concluding chapter is devoted to a brief discussion of some advanced satellite concepts. The treatment of each topic is necessarily brief but is sufficient to provide the general reader with a balanced overall picture of the current situation. The quality of the separate contributions is a little uneven, and there is some occasional overlap between the topics covered, but this does not detract greatly from the value of the volume.

The book is excellently produced with a few photographs and a good number of clear line diagrams. It can be recommended to all requiring a readable and concise background survey of the field.

W. J. G. BEYNON

Modified Nucleosides

The Modified Nucleosides in Nucleic Acids. By Ross H. Hall. Pp. xiii+451. (Columbia University: New York and London, October 1971.) £9.50.

THE concept that ribonucleic and deoxyribonucleic acids are both made up from four nucleoside units is a simplification of the facts. Although RNA molecules are built up largely from four principal ribonucleosides, thirty-four other nucleosides have so far been isolated, especially from tRNA digests. These minor nucleosides are virtually all derived directly from the principal nucleosides, and may therefore conveniently be termed modified nucleosides: many of the latter are simple methyl derivatives of the principal nucleosides but some are more complex modifications. Only five modified deoxyribonucleosides have so far been isolated from DNA digests.

Studies connected with the identification, biosynthesis and function of these modified nucleosides have attracted the attention of biochemists and chemists for a number of years and sufficient data have now been accumulated (many of them by the author himself) to make the publication of a monograph on this subject a welcome event. Professor Hall is to be congratulated on writing an excellent book which will be both a standard text and a practical handbook for research workers in this field. Indeed, this book is strongly recommended to everybody who is interested in nucleic acids.

After a short introduction, there follows a very long chapter (nearly two hundred pages) which is concerned with the physical properties and chemical synthesis of the principal and modified nucleosides (in both the RNA and DNA series) and of the bases derived from them. There is a separate section for each base or nucleoside: melting points, specific rotations (where appropriate), pK_a data, ultraviolet absorption curves and, in some cases, plotted mass spectra are given. There then follows one or more synthetic procedures for each compound, and a section dealing with the occurrence of each modified nucleoside. Although this chapter will be very useful to research workers, it warrants a few minor criticisms. First, although nuclear magnetic resonance (NMR) spectroscopy has been valuable in the elucidation of the structures of what Professor Hall calls hypermodified nucleosides, no NMR data are given. Secondly, in a number of cases, pyrimidine and purine derivatives are represented as lactim (or thiolactim) tautomers although the corresponding lactam (or thiolactam) tautomers are known to be more stable. For a few compounds, both tautomeric forms appear in different parts of the chapter. Finally, while it is a very good idea to

give synthetic procedures, the most useful (and possibly the original) should be emphasized. For example, seven methods are given for the synthesis of adenosine but the first listed would certainly not be the method of choice. In a few cases where only one procedure is given, the method listed is not the best.

There then follows an excellent chapter on the isolation of modified nucleosides, followed by a chapter on the primary structure of tRNA with special emphasis on the relative positions and possible function of the modified nucleosides. The next chapter is concerned with nucleoside modification in DNA. In the following chapter on biosynthesis and metabolism, the evidence for modification occurring at the polymeric level is clearly presented. Chapter 7 deals with various aspects of the chemistry and biology of N^6 -(Δ^2 -isopentenyl)-adenosine (and related compounds) and N -[9- β -D-ribofuranosyl-9H-purin-6-yl]-carbamoyl]-L-threonine. Unfortunately this book went to press too early to include an account of the chemistry of Y riboside, the latest hypermodified nucleoside to be characterized.

The last main chapter is concerned with chemical reactions which can be applied selectively to nucleic acids. Certain aspects of this important subject such as methylation and reduction are particularly relevant to a discussion of modified nucleosides, and thus the inclusion of this chapter is to be welcomed. The book ends with a general summary and a useful appendix on paper chromatographic data. C. B. REESE

Ethology of Sexuality

Sexuality and Homosexuality: The Complete Account of Male and Female Sexual Behaviour and Deviation—with Case Histories. By Arno Karlen. Pp. xx+666. (Macdonald: London, January 1972.) £7.

THE larger part of this competent piece of science journalism is occupied with the history and ethnography of different attitudes toward human homosexual behaviours. The later chapters cover current attitudes on such matters as sex determination, gender roles, endocrine effects and the biological background of sexual identity. The historical and cultural part is lovingly documented but a little confusing in outcome; being confined of necessity to the "overt" culture it offers no basis for any opinion about the comparative prevalence of bisexual manifestations—only about the tolerance or otherwise shown towards them and their popularity as an affectation, a scapegoat, or a source of "otherness". Much of the compilation is recognizably and perhaps excusably at second

hand, and could have done with proper references. Recourse to the original documents would have saved Lord Acton, for example, from having to answer occasionally for the remarks of William Acton, and it would have been interesting to know when and where Havelock Ellis "suggested chastity devices for boys". Granted the size of the book, this may be too much to ask.

The really interesting emphasis in the book—interesting because it will still be unfamiliar to many psychiatrists and counsellors—is ethological: that bisexual potential in humans, and especially in males, though it is undoubtedly an overdetermined behaviour, is far more closely related phylogenetically to bonding behaviour and to dominance than to heterosexuality. It represents one more of the versatile uses to which sex in primates generally, and man in particular, has been put. Psychiatrists who have regarded it as a deviation have missed the fact that the potential for homosexual response is a functional and adaptive behaviour. Exclusive homosexuality is no doubt a problem for its possessor, and (in a culture which rejects it, particularly) associated with personality disorder, but in the generality it is not so much "latent" as a part of a built-in primate potential, a specific adaptation to bonding needs rather than heterosex gone wrong.

From the psychiatric point of view this is an important and unfamiliar, though not original, insight: it suggests that in predominant homosexuality one of the main overdeterminants is connected with dominance. In the light of primatology we need a new look at Adler. Not only is dominance subject to physical, including endocrine, influences, but the Freudian Oedipal conflict reflects a dominance situation between father and son of a special kind. Dr Karlen's acquaintance with depth psychology generally is unfortunately not sufficient for him to complete this line of thought—it would have been worth sacrificing some of the anecdote and all of the "case histories" to a proper consummation of the marriage between primatology and clinical psychodynamics, insofar as that is now possible. As it is, the book is well written, humane and instructive both to professionals and laymen, but it needs a rather steadier hand to complete a serviceable hypothesis.

ALEX COMFORT

Weather by Numbers

Numerical Weather Prediction. By George J. Haltiner. Pp. xvi+317. (Wiley: New York and London, October 1971.) £5.

ALTHOUGH research into numerical weather prediction started in the late

1940s and routine numerical predictions became available to weather forecasters in the late 1950s, texts devoted to expounding the principles and practice are not plentiful. The best so far is *Thompson's Numerical Weather Analysis and Prediction*, dated 1961, and indeed the only other worthwhile text in English since then is *Lectures on Numerical Short Range Weather Prediction*, published in 1969, a very uneven and bulky book which shows all the signs of multiple authorship. There is indeed, then, a welcome for a new book.

The aim of Professor Haltiner's book is stated clearly enough—"to assist students, faculty, and other scientists who presently must rely on highly condensed articles in technical journals"—so we must regard it as a pedagogic book and not one for the specialist. This creates an immediate problem which the specialist, choosing part of the field, avoids. The early research work was concerned with vorticity models; because on the synoptic scale of atmospheric motion the absolute vorticity about a vertical axis is almost conserved and for all practical purposes vorticity is spin, a fairly clear picture of the mechanism is available—one can "see" that columns of air which are stretched will have to spin more quickly and so on. Yet the present day developments are all concerned with dealing directly with the Navier-Stokes and energy equations and the picture is nothing like so clear. The teacher has to decide how much attention to give to the development of vorticity models and how much to the primitive equation models. The problem is heightened because the ancillary mathematics required to integrate the model equations is quite different, the first involving solutions of second order partial differential equations with elliptic boundary conditions and the second the more straightforward but subtle first order hyperbolic equations. Should the student have to learn and understand both?

Professor Haltiner has given about equal space to both, perhaps a good compromise. It allows him to develop the "classical" theory at a leisurely pace, dealing with the equations of motion, the various wave type solutions of the linearized equations, the scale analysis, filtering and the vorticity models with their barotropic and baroclinic instabilities. The author's clarity of exposition, known from his previous writings, is at its best here because the story is a connected one.

The second half of the book dealing with the primitive equation approach was bound to suffer in comparison with the first half. The problems are polarized into three areas, adequately representing the sub-grid scale physics of the

model in terms of larger-scale fields, developing a suitable integration scheme and obtaining a good starting point for the integrations. Only the first of these is really meteorological in character while the latter two are decidedly in the field of numerical analysis. Moreover, no single solution to any of these problems has been found acceptable to everyone, which forces Professor Haltiner to pick and choose among the many solutions which have been advanced without any very clear reason for choice except familiarity. Nevertheless he has managed to include some illustrative material on nearly all the principal aspects such as radiative transfer, cumulus convection, finite difference schemes, objective analysis and so on, enough to start the student thinking without going into any great depth.

With no real competitor covering the same ground with this crisp approach, Professor Haltiner's book should be in great demand by students and teachers, for the subject matter is becoming a very important part of the meteorological teaching syllabus.

E. KNIGHTING

Rare Gases

The Inert Gases: Model System for Science. By B. L. Smith. Pp. xii+172. (Wykeham: London, June 1971.) £2.50.

IN these days of specialization where volumes may be written on topics, it is no mean feat to give a comprehensive survey of a small area in science in 172 pages. In his book on the rare gases Dr Smith carries out this operation most successfully. This well-laid-out book follows the rare gases from their discovery to their multifarious present day applications in the physical and—very surprisingly—biological sciences.

The theme of the book is how the rare gases are used as models in physics because of their simple physical properties. They are monatomic, extremely stable chemically, have spherically symmetric electron charge clouds, and interact with one another in a particularly simple fashion. Thus chapters are devoted to theories of the gaseous, liquid and crystalline phases with the rare gases as the physical counterparts of the theoretician's abstractions. The interplay between theory and experiment is constantly emphasized. A further chapter on critical phenomena gives an excellent account of present work on the liquid-vapour transition and the analogous ferro-magnetic transition, and a discussion of optical and dielectric properties completes the study of the rare gases in physical theories. A small chapter on their chemistry points out that they may take part in chemical

reactions and form stable chemical compounds. Finally, there is a description of the applications of the rare gases. Apart from their better known uses in lasers or in radioactive dating, one of the most novel and interesting uses of these gases is in medicine, in which they can apparently be used under pressure to induce total anaesthesia in man. Experiments on this are being used to establish a theory of anaesthesia. Other applications in biology are also described.

A minor criticism of the book is that some of the theory described in it is too sophisticated for first year undergraduates and sixth-formers for whom the book is intended. Further, some of the statements made are misleading. For example, at the bottom of page 35 it is implied that diatomic gas molecules do not rotate. On page 30 it is stated that ^4He does not have a triple point, whereas the phase diagram of ^4He shown on the same page clearly shows two triple points. These are minor blemishes, however, and the book makes a fine introduction to the rare gases for scientists at any level.

I. J. ZUCKER

History of Science

The Science of Matter: a Historical Survey. Edited by M. P. Crosland. Pp. 440. (Penguin: Harmondsworth, 1971.) 70p.

Steps in the Scientific Tradition: Readings in the History of Science. Edited by R. S. Westfall and V. E. Thoren. Pp. xii+544. (Wiley: New York and London, October 1971.) £3.50 cloth; £1.75 paper.

THE title of neither of these books makes its content clear. Crosland's title is the better chosen. There are 163 short extracts from important papers or books reporting original discoveries and theories, or from important critical estimates of the state of some branch of science bearing on the central theme of the constitution of matter. They are divided into some thirty groups beginning with "Theories of Matter in Ancient Greece" and ending with "Symmetry and Anti-Matter". Each group is prefaced by a short informative introduction. The total effect is one of a stimulating record of the evolution of an important aspect of man's attitude to his material circumstances.

Dr Crosland observes no boundaries of disciplines. Naturally in antiquity he has to start with the matter speculations of the Greeks, which fit into no conventional category of chemistry or physics. He includes in matter theory enough biology and astronomy to show that as a historian he himself is entirely in sympathy with the modern approach to experimental materials science in its

disdain of the nineteenth century classification of study. So, with a comprehensiveness which Aristotle would have applauded, Dr Crosland ranges over the works of Newton, Proust, Lamarck, Dalton, Joule, Robert Brown, Huygens, Claude Bernard, Schwann, Kirchhoff, Einstein, Crick, ending with Dirac and Yang. Physical matter, organic matter, anti-matter: to the historian with an eye to see, it is all one story.

The extracts are necessarily short but Dr Crosland has a flair for picking out what is both important and intelligible. The material is well documented and there is a good guide to further reading. The result of what seems to have been conceived as merely an auxiliary text turns out to be a book which, in the hands of the right teacher, could be an excellent textbook for a general course in the history of science.

Paradoxically, the Westfall and Thoren book, which was planned as a textbook for a class course, does not seem nearly so likely to guide either a teacher or his class. There are twenty-two long passages from Aristotle, Ptolemy, Lucretius, Roger Bacon, Buridan, Galileo, Harvey, Descartes, Newton, Franklin, Lavoisier, Playfair, Young, Carnot, Schwann, Darwin, J. J. Thomson, T. H. Morgan, and Langmuir. Each passage is prefaced by a reflective note on its significance and on the historical lessons which may be learned from it. No doubt it may be an excellent thing for any student, who may have heard references to the celebrated thirty-first query in Newton's *Opticks* and even be familiar with odd quoted sentences from it, to read the whole of that marvellous chapter in the theory of matter. If he relies, however, on the editor's brief introductory note to explain why it is so marvellous, he will be left doubting, because each note only sketches lightly the intellectual situation in respect of one problem or contemporary question. A good teacher will undoubtedly explain the antecedents, the composition, the reception and ultimate influence of each passage, and the editors say that they do in fact leave the use of the book to the teacher. Why then just pick out these far from comprehensive passages and expect some unknown teacher to make a course out of them unaided?

Teachers of the history of science need help just as much as any other teachers, and this selection would have made far more sense if we had at least been told what end result its editors had got out of using it themselves, and how they had linked passage with passage. These are, in any case, too few to provide any broad sweeping view of the "scientific tradition".

The contrast between the two books tells us something important. The teach-

ing of the history of science, if it is to carry any weight inside or outside the curriculum, needs the same vision of the whole as the effective teaching of science itself. The reputation of the Indiana school is high enough for us to be certain that Westfall and Thoren have such a gift, but their book does not transmit it to teachers outside. Crosland's more modest effort achieves more, shows him to possess the wider view of science as a whole, and to be able to lend his vision to others. Experienced teachers may find the Westfall-Thoren book useful. They might well find the Crosland book almost inspiring.

FRANK GREENAWAY

Computing Chemistry

Computer Handling of Chemical Structures. By Micheal Lynch, Judith M. Harrison, William G. Town and Janet Ash. Pp. xii+148. (Macdonald: London; Elsevier: New York, 1971.) £2.

THIS book represents a first in bringing together a brief but comprehensive overview of methods of handling chemical structure information. The first six chapters give an accurate and concise description of the various methods in use today. The descriptions are detailed enough to give the reader an indication of the philosophy and details of how each method works. The bibliography at the end of each of these six chapters provides access to those papers which represent the major work in each of the areas. The same excellent balance between detail and brevity is maintained in chapters eight and nine in which the implementation of these methods in both the publishing and industrial environments is described. Here the reader can better discern the value and limitations of each system. Unfortunately very little work has been done in identifying the system requirements met by each of the various methods, and this weakness is reflected in the general nature of chapter seven on system requirements. As the reviewer reached this chapter he had hoped to find the same incisive analysis which had been demonstrated in the earlier chapters. The last chapter outlines several areas where chemical structure information methods can have their greatest impact. The authors failed to mention in this chapter the obvious need to relate structural characteristics to chemical and biological properties.

This well written small volume should be required reading for anyone using the chemical literature, especially graduate students. C. M. BOWMAN

People of New Guinea

Place and People: an Ecology of a New Guinean Community. By William C. Clarke. Pp. xii+265. (University of California: Berkeley, Los Angeles, and London, November 1971.) \$9; £4.30.

THE author, an American geographer, presents a micro-region study of a "habitat on the edge of human settlement", a remote part of the Bismarck Range of Australian New Guinea. In 1964-5, the time of the study, 154 people occupied the heart of the Ndwimba Basin, making most of their living—except for a trickle of traded luxuries—from the resources of a few square miles. The first recorded contact, an Australian patrol, occurred only six years before, but when the research began it was already necessary to take steel tools and future road-building projects into account. Evidently the two clans of the Ndwimba Basin will not remain long on the edge.

The book is well titled for a study of an ecosystem "... considering human activities and the physical environment as truly interdependent parts of a single system". With much detail of terrain, soils, weather, plant cover, crops, game, and domestic animals Clarke depicts the spatial disposition of Ndwimba people and their activities: gardening, husbandry, hunting, communicating, and collecting materials for food and fabrication. There is a continuous assessment of (1) the inhabitants' views of the habitat in light of (2) the observer's views, and of (3) the decisions and expectations of inhabitants in light of (4) the observable or predictable effects of their decisions: dietary variety and sufficiency, work schedules and yields, the minimization of risk, environmental changes, and the maintenance of community.

The study is rich in immediacy. In each of several detailed instances a specific individual is shown deciding on the location of a specific clearing, with particular crops in view, particular partners or helpers. In one case a specific tree is found growing in the new swidden, the deceased planter recalled, the tree spared for its eventual product. The predilection of individual men for moving about the countryside is noted, the purely aesthetic appeal to them of certain localities, and the ecological implications of their having numerous scattered gardens. To borrow the author's words about the value of studying micro-regions, there emerges "... a vivid and accurate image of what is present and what is happening [in one part] of the wider region ... thus lead[ing] to a deeper understanding of the diversity of life and environment in any region and ... the recognition of the important regional consistencies".

The physical domain of a small group

of New Guinea gardeners is well realized, full of animals and plants, locations and soils, and of choices and activities for utilizing them. The resident's deep attachment to place is better projected than in most ethnographic monographs devoted to social structure or ritual. Clarke's model is that of a total of varied individual agents rather than a monolithic order that submerges them. Husbandry (or hunting) may seem to some a bit neglected, but one must keep in mind the rich and obtrusive New Guinea plant world, doubtless a more obvious measure of the condition and use of the Ndwimba environment, above all by gardeners.

The aims of the book are modest and sensibly achieved, with no claim to opening up new theoretical vistas. Clarke amply justifies his choices among vistas already open in providing what he himself calls "a qualitative sketch" of a New Guinea people in their place and in evaluating the ecological future of these shifting cultivators whose niche, at present stable and diverse in life forms, may well with impending progress narrow toward uniformity and lessening stability. JAMES B. WATSON

Arctic Ecology

Animals of the Arctic: The Ecology of the Far North. By Bernard Stonehouse. Pp. 172. (Ward Lock, London, October 1971.) £2.60.

ARCTIC ecosystems are receiving more attention, particularly public attention, than ever before. The daily and weekly press is constantly telling us that the tundra and its flora and fauna, the lakes and forests of the north, and the Arctic seas, are threatened by the oil industry, radioactive fallout, and pesticides, and that the northern ecosystems are especially delicate or "fragile". Perhaps they are, and it is good that the alarms are sounded, but the fragility still has to be demonstrated. Let us hope the demonstration can be made, one way or the other, and in a scientific manner, while there is still time.

Against this background of urgency Dr Stonehouse's book is a timely presentation of the life and the environment of the Arctic for the benefit of the general public, and it is a good example of scientific description and explanation in plain and non-technical terms. The photographs and drawings form a very important part of the book (it is almost a "coffee-table" book), and they are excellent, so good that they could no doubt sell the book by themselves. One would like to know more about the photographers and the artists, beyond the single name alongside each illustration. The text is factual and often a little dry to the palate, but there is no doubt of

the wealth of information displayed, or of the sound ecological principles by which it is presented. There are certain high points that strike the reader, such as: "There is an appealing biological economy about Arctic organisms. . . . There is none of the ragbag clutter of the tropics, where thousands of species jostle for space and ecology is a tangled net . . .". Perhaps a little partisan, but very well said.

The author clearly knows the literature up to the minute, and his book is free from those little mis-statements of fact which infuriate the expert and tempt small minds to point them out with glee, although several controversial issues, such as the famous lemming cycles, the details of the Pleistocene glacial oscillations, and the function of walrus tusks, are perhaps simplified too much, giving the impression that they have been settled once and for all. As a Canadian, I was distressed to see the Canadian Arctic Islands described as lying "north of Canada", which reminds one a little of Sir Leopold McClintock's remark in the first decade of this century that Otto Sverdrup had stopped the northward expansion of the British Empire in North America. But these are small points to quibble about in a work of this high standard. The chapter on the changing polar climate, and the climatic history of the north, is particularly good. The last chapter, on "Man in the Arctic", is good but too short; one would have liked to have this theme developed somewhat, in view of the present anxieties.

I am red-green colour blind, as many men are. I was unable to distinguish between the colours in the Arctic-Subarctic map, and some of the colours in the illustration of the distribution of seals. On consultation with friends of normal colour vision I found that they had trouble too. Perhaps in the second edition this could be remedied.

This is a handsome, authoritative book, and excellently produced. It should sell well. M. J. DUNBAR

Quantitative Sanity

Lectures on Biostatistics. By D. Colquhoun. Pp. xviii+425. (Clarendon: Oxford; Oxford University: London, November 1971.) £5.50 boards. £2.75 paper.

A FEW years ago, many books on applied statistics were inadequate, irrelevant to real problems, or even actively misleading. Standards are now higher; although these major faults have not wholly disappeared a more frequent weakness today is a general dullness. Dr Colquhoun's book is a refreshing exception. He writes as a pharmacologist with long experience in the use of

statistical method but with no claim to theoretical expertise. When he entitled Section 1.1 "How to avoid making a fool of yourself", he set the tone for the whole book. He neither regards statistics as a set of rules for blind application nor contemplates with awe a mathematical edifice; for him, biostatistics is a pattern of thought and analysis to aid the biologist in understanding his data, not a substitute for reason.

Dr Colquhoun serves a generation of biologists not completely averse to mathematical argument, and he gives them a modicum of algebraic explanation. Occasionally he may seem to be whistling in the dark to preserve his own courage in the face of mathematics, but in places—notably in his discussion of variances of functions—he presents admirably concise algebraic support for his methodology at a level suited to his readers.

The book covers much of the standard material on distributions, tests, and estimations, with greater emphasis on the practice of regression, calibration curves, bioassay, and non-linear estimation than is usual. The early chapters betray excessive addiction to nonparametric methods, in spite of their unsuitability for the later, more interesting, problems of estimation; the strange notion that "there is usually no reason to prefer the mean to the median" appears once more. Nevertheless, the presentation of nonparametric techniques is essentially practical and consistent, until more complex problems compel a switch to the usual Gaussian models. The chapter on curve-fitting and regression is an admirable account of a difficult topic; simple examples illustrate well the meaning of least squares, the process of minimization, the consequences of reparameterizing, and the difficulties introduced by non-linearity. Throughout the book, the author shows an understanding of the use of computers and a welcome awareness of the dangers inherent in uncritical use of standard packages. A little oddly, he seems to attribute the emphasis that statisticians place on linear models to their aesthetic delight in matrix algebra.

A biologist who studies this book may not find all he needs, but he will certainly be led away from folly.

D. J. FINNEY

Petroleum

Geology of Giant Petroleum Fields. Edited by Michel T. Halbouty. (A Symposium of Papers on Giant Fields of the World, including those presented at the 53rd Annual Meeting of the Association in Oklahoma City, Oklahoma,

April 23–25, 1968.) Pp. viii+575. (The American Association of Petroleum Geologists: Tulsa, Oklahoma, 1970.)

WHEN this volume was published, a large number of petroleum geologists must have been, with the reviewer, surprised (agreeably) to read in Table 1 that the nineteenth largest oilfield in the world was the Ekofisk Field in Norwegian North Sea waters, with estimated recoverable reserves of 7,000 million barrels. After developments in 1971, not only has this estimate been confirmed, but new important oil discoveries have been made in the British sector of the northern North Sea. It seems probable that the British Petroleum Forties Field may be considerably larger than Ekofisk. BP Ltd have very recently announced that oil production from this field is likely to rise to 400,000 barrels per day—about one-fifth of Britain's present consumption. Such a dramatic change in the petroleum reserves of a country can only come from the discovery of giant oil or gas fields, and this latest example amplifies the theme of this book—namely, that a very large proportion of the world's reserves of hydrocarbons are contained in large individual accumulations. As the editor points out, the almost freakish natural imbalance of petroleum reserves in the present economic dominance of these fuels divides the nations into "haves" and "have nots", just as the imbalance of coal and iron ore deposits did in older times, but with a very different distribution. Oil reserves mean economic and political power—facts which economists and politicians of both "haves" and "have nots" are only now beginning to realize to the full. The romantic figure of the new generation Arab, exchanging his desert robes and camel for western-style military uniform and Cadillac, and flexing his extortionist muscles, is matched by the less familiar figure of the coal and iron age magnate searching disconsolately in his wardrobe for the tattered cloak of a petroleum "have not".

The book does not shirk the problems of definitions and assessment of economic value of reserves of petroleum. The accuracy of reserve estimates—particularly recoverable reserves—depends on drilling and production data density, which in turn reflects the stage of development of the oil or gas field. The US with about 23,000 oil and gas fields tends to rely almost exclusively on well data, whereas the USSR with only 1,118 fields is in a much more primitive stage of development and has to rely on estimates based on one discovery well only. The book states that what it offers in this respect is an indication of order of magnitude.

One significant departure of the book from previous discussions of the same

problem is the escalation of scale from 100 million barrels to 500 million barrels of oil and from one trillion cubic feet to 3.5 trillion cubic feet as defining the lower limit of "giant" fields. This is necessary because there are too many fields on the older definition to handle within the scope of the book—many of which, incidentally, would not be economic to develop in Alaska or in the northern North Sea.

The editor in his introduction points out that reserves do not have the same value irrespective of location. Proximity to markets makes them more valuable. Remoteness, and extremes of environment (=cost of development) greatly increase the size of accumulation which will be economic. All that can be simply said is that very large fields will pay wherever they are, and this fact emphasizes the purpose of this book, which is to establish guidelines—both empirical and scientifically deduced—pointing to the fundamental geological factors which lead to the accumulation of oil and gas in large fields.

The approach to the problem is a well-tryed one. It starts with twenty-seven papers describing and analysing the giants of productive regions (for example, US, Mexico, Venezuela, and so on) or the case histories of famous individual giants both old and new (for example, Oklahoma City, Gröningen and Sarir). These case histories are well balanced in terms of the wide variety of sedimentary, stratigraphic and structural conditions, but understandably not so well balanced from a regional or total reserves point of view. The treatment of the Middle East is totally inadequate, no doubt because either developers or governments will not allow open disclosure or discussion.

The book concludes with a chapter of analysis, first, of the geological factors which control the occurrence of giants and, second, proposes a classification of the world's sedimentary basins. The former is admirable and would not find many dissenters among the ranks of thinking explorationists. This more or less tells us what to look for. The basin classification—with the maps of productive regions—attempts to guide us where to go to explore for giants. This is less successful, perhaps unnecessarily complicated, with palpable errors which cannot be discussed here, and in any case is highly controversial.

The science of petroleum exploration is, like many others, at a stage where it is bemused by the plethora of descriptive detail and highly individual speculative theory. It badly needs works of synthesis like this book which is wholly admirable and useful not only to industrial explorationists and management, but is invaluable to teachers and students of the subject. W. D. GILL

CORRESPONDENCE

Exposure to Asbestos

SIR,—Your article "Exposure to Asbestos" (*Nature*, 234, 383; 1971) quoting work in a USA shipyard gives the impression that the present standards for maximum permitted levels of asbestos dust emission are too high.

Until 1968 the maximum permitted level for asbestos dust concentration in work areas in the USA was expressed in accordance with the standards of the American Conference of Government and Industrial Hygienists in millions of particles per cubic foot. The standard during the time at which the ship repair workers that you have reported were exposed was therefore the pre-1968 standard of 5 million particles per cubic foot.

Since asbestosis was not diagnosed in persons with less than 10 years of cumulative exposure, the only relevant dust counts are those for the pre-1961 period. The average level of dust concentration aboard ship where 98% of the man hours were spent, given in the *New England Journal of Medicine*, by the test method appropriate to the standard, was 7.2 m.p.p.c.f., in 1965. For the only previous year quoted, 1945, the measurement, while taken by a different method, indicates levels nearly twice as high.

In 1968 the American standard was reduced from 5 m.p.p.c.f. to 2 m.p.p.c.f. or to 12 fibres/millilitre, since they regarded these as roughly equivalent.

The current threshold limit value in the USA is a time weighted average of 5 fibres/millilitre over an 8 h period with a peak not exceeding 10 fibres/millilitre in a 15 min period. In the UK the Factory Inspectorate in interpreting the Asbestos Regulations 1969 has adopted a TLV of 2 fibres/millilitre and for concentrations between 2

and 12 fibres/millilitre over a 4 h period takes into consideration the level of concentration and duration of exposure.

Thus the levels at which the full provisions of the regulations are applied are in both countries well below the levels of shipboard exposure for pipe coverers on which you have reported.

Yours faithfully,

W. P. HOWARD

*The Asbestos Information Committee,
10 Wardour Street,
London W1V 3HG*

Heads in Bags

SIR,—After *Nature's* excellent commentary on the Compton Report it was sad to find a scientist—Harald Trefall (*Nature*, 235, 347; 1972)—dealing so unscientifically with a more human problem. I would like to remind Mr Trefall of the point of the enquiry. If our civilized standards of justice are to mean anything, they must be defended against corruption by the sort of violence that they are supposed to be fighting. I am proud that my countrymen will go to considerable, though unhappily inadequate, lengths to maintain the standards of British justice. I am saddened that our forces of "law and order" act as though they are above the law; it is even sadder that Mr Trefall does not see the paramount importance of this.

Mr Trefall should also realize that if political arguments are to be settled by exchanging atrocity stories, much time can be saved by picking sides according to nationality—Irish or English, Israeli or Arab, and so on. If Mr Trefall were to study the recent history of Ireland, he would discover that the forces of "law and order" have seldom acted

according to the standards of civilized justice, which gives some point to the resistance of many Irishmen to the forcible imposition of that same law and order. The concept of the justice of overthrowing tyranny by force is old and honourable—see the American Constitution. The blind worship of authority which Mr Trefall apparently advocates is even older, but much less honourable.

Yours faithfully,

R. W. FAKES

*Biochemistry Department,
University College,
Gower Street,
London WC1*

Semmelweis in Translation

SIR,—In a review by E. Gaskell of *A History of Medicine* (edited by Lester S. King; Penguin: Harmondsworth, 1971; 60p) which appeared in *Nature* of February 4, 1972, page 290, is a statement which implies that the works of Semmelweis have never been translated. This is not true, for I have read a translation, by F. P. Murphy, of *Die Aetiologie, der Begriff und die Prophylaxis des Kindbettfiebers* (Vienna: Hartleben, 1861) which appeared in *Medical Classics*, 5, 350–773 (Baltimore: Williams and Wilkins, 1941).

Yours faithfully,

C. E. D. TAYLOR

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Obituary

Professor Emmanuel Fauré-Fremiet

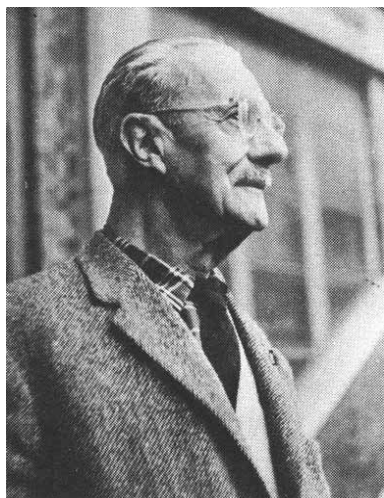
PROFESSOR EMMANUEL FAURÉ-FREMIET, cytologist, developmental biologist, and protozoologist, died on November 6, 1971, in Paris.

Born on December 29, 1883, as the

older son of the composer and organist Gabriel Fauré, Emmanuel spent much of his youth with his maternal grandfather, sculptor Emmanuel Fremiet, whose name both he and his brother adopted in the compound Fauré-Fremiet.

For 60 years Fauré-Fremiet was

associated with the Laboratoire d'Embryogénie Comparée, which became in 1955 the Laboratoire d'Embryologie Expérimentale, of the Collège de France. He took the chair there in 1928, succeeding his father-in-law, and stayed there until his retirement in 1955. As "Professeur



Courtesy of Mme Marie Fauré-Fremiet

honoraire", he continued in active research at the Collège de France and at Gif-sur-Yvette until his death. In 1929, 1933, and 1950, with the aid of Rockefeller Foundation and Commonwealth Fund grants, extensive trips were made to North and South America, with a short, final visit to the United States in 1970.

Fauré-Fremiet's impact on science was as a theorist. His concepts and hypotheses have been as highly original as they are heuristic, whether in the field of protein chemistry or systematic protozoology.

A synthesizer and an innovator, he was also a pioneer in many of his observations—in his early work on protozoan contractile fibres (1904), his discovery of mitochondria in protozoa (1910), his study on the nature of collagen (1920s), and his early recognition of the evolutionary unity of diverse groups of the ciliate protozoa through common properties, both static and dynamic, of their infraciliature. Over 70 when he first took up electron microscopy, he instantly became a world leader in ultrastructural biology, once again comprehending the overall picture as well as producing superb electron micrographs—many of which are still unpublished—of formerly unknown or poorly understood cytoplasmic structures.

In his own research, and in that of his students and laboratory guests, Fauré-Fremiet contributed to four principal areas of biology: cytology, with emphasis on cellular constituents as revealed by light and, later in his career, electron microscopy; developmental biology, including experimental embryology, tissue culture, and diverse problems of growth and development; the physico-chemistry of fibrous proteins, a subject holding fascination for him throughout his active scientific life; and ciliate protozoology. The last area, to which Fauré-Fremiet devoted his

greatest efforts during the last twenty-five years, may be subdivided into at least four parts: experimental morphogenesis, ecology, phylogeny and evolution and systematics. Most of his 500 publications deal with protozoological problems.

In all his works, although he gathered many original data from both field and laboratory observations, his most memorable contributions are in the realms of synthesis and of innovative hypotheses. Great embryologists, for example—men like Paul Weiss and the late Ross Granville Harrison—have mentioned how they were excited by Fauré-Fremiet's little-publicized book, *La Cinétique du Développement*, when it appeared in 1925.

An accurate measure of this modest but highly intellectual man's impact on the scientific world may be seen in the long list of honours conferred on him during his lifetime. He was active in many biological societies in France and abroad, but his principal honours were the elections to membership of the most prestigious academies and learned societies in the world. He was a Membre de l'Institut de France, Académie des Sciences, Foreign Fellow of the Royal Society, Foreign Associate of the National Academy of Sciences, Membre Etranger de l'Académie Royale Flamande des Sciences, des Lettres et des Beaux Arts, Membro Straniero della Accademia Nazionale dei Lincei, Honorary Foreign Member of the American Academy of Arts and Sciences, and Membro Correspondente da Academia Brasileira das Ciências. In the field of protozoology, as might be expected, Fauré-Fremiet was active in both national and international societies and congresses. He was elected an Honorary Member of the Society of Protozoologists, and Honorary President of the Second International Conference on Protozoology, held in London in 1965. He was also a founder member of the *Groupe-ment des Protistologues de Langue Française* in 1961.

But Fauré-Fremiet was not simply a scientist. Inheriting the artistic abilities of his grandfather Fremiet, he produced several sculptures of value, some of which now stand in the parks and museums of Paris. In his younger days he also painted, and his graceful, lifelike sketches of species of protozoa, many of which are unpublished, are reminiscent of animal drawings made by his grandfather. He was also much in demand as a writer of obituaries for the many colleagues he outlived.

But, as well as being highly creative, Fauré-Fremiet could also be an extreme perfectionist—a quality not without its problems. The story is told that, in 1929, the late Maurice Caullery sent off to press the manuscript of a book

on cytology prepared by Fauré-Fremiet while the latter was abroad for several months. When he returned, Fauré-Fremiet was most upset and immediately withdrew the work from the publisher, with the comment that he must not only add a little new information to it, but also reshape the entire draft. The book never did appear.

Students or close associates numbered many over Fauré-Fremiet's long career, and numbers of them have gone on to establish their own reputations. A great friend to his fellow scientists, Fauré-Fremiet always had time for the questions of his students and colleagues.

Fauré-Fremiet married twice, although he died childless. In 1913 he married Jeanne Henneguy, daughter of Louis-Félix Henneguy the cytologist. Mme Fauré-Fremiet died in June 1967, and four years later, a mere five months before he died, Fauré-Fremiet married his secretary and research collaborator, Mlle Marie Hamard, who survives him.

Protozoologists, embryologists, and all who knew him will deeply mourn the loss of such a leader in science and a man of great humility and sensitivity.

Announcements

University News

Mr Maurice Graneek, PIRA, Leatherhead, has been appointed to the Bentley chair of manipulative machinery in the Department of Mechanical Engineering, **Loughborough University of Technology**.

Dr Jack Stevens, University of Chicago, has been appointed to the chair of orthopaedic and traumatic surgery, **University of Newcastle upon Tyne**.

Mr A. M. Walker has been appointed to a personal chair in the Department of Probability and Statistics, **University of Sheffield**, and **Dr R. J. Connolly** has been appointed to the second chair of psychology.

Miscellaneous

The **Institution of the Rubber Industry** has awarded the Colwyn Medal for 1971 to **Professor J. D. Ferry**, University of Wisconsin, and the Hancock medal for 1971 to **Dr E. R. Gardner**. **Dr William C. Wake** has accepted an invitation to deliver the Foundation Lecture in 1973.

Mrs B. P. Hall, British Museum (Natural History), has won the Stamford Raffles award of the **Zoological Society of London**, in recognition of her work on the taxonomy and zoogeography of birds. The Society's scientific medal has been awarded to **Professor D. L. Lee**, University of Leeds, for his work on parasitology, and to **Dr P. L. Miller**,

University of Oxford, for his work on neurophysiology; the Thomas Henry Huxley award has been made to **Dr Richard D. Jurd**, University of Southampton, for his doctoral thesis "The haemoglobins of *Xenopus laevis* (Daudin): their characterization, ontogeny, and the control of their synthesis".

Nominations are invited for the first annual award—£500 and a trophy—for the best contribution in the field of **medical journalism** during 1971. The award scheme is sponsored by Ortho Pharmaceutical Limited and the judges include Dr E. V. Kuenssberg, chairman of the council of the Royal College of General Practitioners, Mrs Marjorie Proops, a journalist, and Mr Paul Vaughan, broadcaster and deputy editor of *World Medicine*. Further information can be obtained from the Medical Journalists' Association, 2 Keble Road, Maidenhead, Berkshire SL6 3BA.

An award of 5,000 Swiss francs will be made during 1972 for the best study submitted to the **International Health Foundation**, Geneva, on "The psychology of the patient with a skin disease". An additional prize of 2,000 Swiss francs may also be awarded for the best paper submitted by an author under 35 years old. Further information can be obtained from the International Health Foundation, 1 Place du Port, 1204 Geneva, Switzerland.

Nominations are invited by the **American Psychological Foundation** for the 1972 national media awards, which are presented annually for outstanding reporting which increases the public's knowledge and understanding of psychology. The awards are made in three categories: for newspaper reporting; for a television or radio programme or a film; and for a magazine article, book or monograph (not a textbook). Further information can be obtained from the Public Information Officer, American Psychological Association, 1200 Seventeenth Street NW, Washington DC 20036, USA.

International Meetings

March 18, **Careers in Mathematics**, London (Secretary and Registrar, Institute of Mathematics and its Applications, Maitland House, Warrior Square, Southend-on-Sea, Essex SS1 2JY).

March 20–23, **Recent Advances in Bio-medical Engineering**, Liverpool (J. D. Gasking, Department of Pharmacology, The Medical College of St Bartholomew's Hospital, Charterhouse Square, London EC1).

March 22, **Modern Mathematics in Schools in Relation to the Needs of the Professions**, London (Secretary and Registrar, Institute of Mathematics and its Applications, Maitland House, Warrior Square, Southend-on-Sea, Essex SS1 2JY).

March 23, **University-Industry Cooperation in Control and Automation**, London (Secretary, IEE, Savoy Place, London WC2R 0BL).

March 25, **Transition from Schools to Universities and Polytechnics**, York (Secretary and Registrar, Institute of Mathematics and its Applications, Maitland House, Warrior Square, Southend-on-Sea, Essex SS1 2JY).

March 27–28, **High Speed Photography**, Englefield Green, Surrey (C. W. Husband, c/o Central Unit for Scientific Photography, Royal Aircraft Establishment, Farnborough, Hampshire).

April 5, **Exploration Geochemistry**, London (Society for Analytical Chemistry, 9–10 Savile Row, London W1X 1AF).

April 12, **Atomic Spectroscopy in Ceramic Analysis**, Keele (Society for Analytical Chemistry, 9–10 Savile Row, London W1X 1AF).

April 17–18, **Calorimetry in the Biological Sciences**, Birmingham (Administrative Officer, British Biophysical Society, 7 Warwick Court, High Holborn, London WC1R 5DP).

April 20, **High Performance Liquid Chromatography in Columns**, Newcastle upon Tyne (Society for Analytical Chemistry, 9–10 Savile Row, London W1X 1AF).

April 20–21, **Annual Congress and Scientific Exhibition of the British Institute of Radiology**, London (General Secretary, British Institute of Radiology, 32 Welbeck Street, London W1M 7PG).

April 20–21, **Fundamental Aspects of Ion Movement in Anodic Films**, Nottingham (Dr P. H. G. Draper, Department of Chemistry, Chelsea College of Science and Technology, Manresa Road, London SW3 6LS).

April 21, **Diffraction Gratings** (Meetings Officer, Institute of Physics, 47 Belgrave Square, London SW1X 8QX).

April 21–22, **Protein Metabolism and Hormones**, Southampton (Dr J. D. Sutton, National Institute for Research in Dairying, Shinfield, Reading RG2 9AT).

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

UKAEA: Research Group. Report 6923: Radioactive Fallout in Air and Rain: Results to the Middle of 1971. By R. S. Cambray, Miss E. M. R. Fisher, W. L. Brooks and D. H. Peirson. Pp. 46. (Harwell: Health Physics and Medical Division, Atomic Energy Research Establishment, 1971. Obtainable from HMSO.) 40p. [1612]
Medical Research Council. Monitoring Report No. 18: Assay of Strontium-90 in Human Bone in the United Kingdom—Results for 1969. Pp. iii+16. (London: HMSO, 1971.) 18p net. [1712]
Alpha and Omega, Book 3. By M. S. Rattue. Pp. 20. (Reigate: M. S. Rattue, 1971.) [1712]
Teacher Training Opportunities for Science, Technology and Mathematics Graduates. Pp. 93. (London: The Royal Society, 1971.) [2012]
Department of Education and Science. Animals Act, 1964 (Restriction of Importation—Report of

the Advisory Committee for 1970. Pp. iii+22. (London: Department of Education and Science, 1971.) gratis. [2012]

The Fertiliser Society. Fertiliser Caking and Its Prevention. By D. C. Thompson. Pp. 45. (London: The Fertiliser Society, 1971.) [2112]

Building Research Station Current Paper, 35/71: Wind Damage to Buildings in the United Kingdom 1962–1969. By J. B. Menzies. Pp. 9. (Garston, Watford: Building Research Station, 1971.) [2112]

Department of the Environment. Forest Products Research. Bulletin No. 56: The Growth and Structure of Wood. By B. J. Rendle. Revised by J. D. Brazier. Pp. 15. (London: HMSO, 1971.) 42p net. [2112]

London and Home Counties Regional Advisory Council for Technological Education. Bulletin of Special Courses—Short Advanced Courses in Technology Management Studies and Commerce in the Region, 1971/72, Part 2: Spring and Summer Terms. Pp. 108. (London: London and Home Counties Regional Advisory Council for Technological Education, 1971.) 60p. [2112]

Recent Developments in Psychogeriatrics—a Symposium. Edited by D. W. K. Kay and Alexander Walk. (*British Journal of Psychiatry*, Special Publication No. 6.) Pp. 125. (Ashford, Kent: Headley Brothers, Ltd., 1971. Published by authority of the Royal Medico-Psychological Association.) £1.60; \$4.25. [2112]

Proceedings of the Royal Irish Academy. Vol. 71, Section B, No. 15: Interfacial Marine Formation and Lateglacial Freshwater Formation in Shortlough Townland, Co. Wexford. By E. A. Colhoun and G. F. Mitchell. Pp. 211–246. 44p. Vol. 71, Section B, No. 16: Michael Addition Reactions with Acetylene Esters and Ketones. By K. Bugge, G. P. Hughes and Eva M. Philbin. Pp. 247–256. 16p. (Dublin: Royal Irish Academy, 1971.) [2112]

A Medical School for Hull. (A report prepared by the Foundation Committee for the proposed Medical School for the University of Hull.) Pp. 36. (Hull: The University, 1971.) [2112]

Journal of Applied Electrochemistry, Vol. 1, No. 1, February 1971. Edited by Dr D. Inman. Published Quarterly. Pp. iii+1–78. Subscription rates: 1971 volume (4 issues) £10 (plus surface delivery 25p); Single copies £3 (delivery 8p). Airmail rates on application. (London: Chapman and Hall, 1971.) [2112]

Imperial College. Annual Report 1970–71. Pp. vi+96. Annual Accounts 1970–71. Pp. 31. (London: Imperial College, 1971.) [2112]

National Parks and Access to the Countryside Act of 1949; Countryside Act of 1968. Fourth Report of the Countryside Commission for the year ended 30 September 1971. Pp. vi+70. (London: HMSO, 1971.) 68p net. [2112]

Philosophical Transactions of the Royal Society of London. A: Mathematical and Physical Sciences. Vol. 270, No. 1209 (16 December 1971): Determination of the Thermal Conductivity of Toluene—a Proposed Data Standard—from 180 to 400K under Saturation Pressure by the Transient Hot-Wire Method. I. The Theory of the Technique. II. New Measurements and a Discussion of Existing Data. By E. McLaughlin and J. F. T. Pittman. Pp. 557–602. £1.20; \$3.10. Vol. 270, No. 1210 (16 December 1971): Tides and Waves in the Vicinity of Saint Helena. By D. E. Cartwright. Pp. 603–649. £1.25; \$3.25. (London: The Royal Society, 1971.) [2112]

University of Birmingham. Science and Engineering Postgraduate Prospectus 1972. Pp. 80. (Birmingham: The University, 1971.) [2212]

Catalogue of Fossil Hominids. Part 2: Europe. Edited by Kenneth Page Oakley, Bernard Grant Campbell and Thea Ivitsky Molleson. Pp. xii+379. (London: British Museum (Natural History), 1971.) £11.50. [2212]

Department of Education and Science. Statistics of Education 1970. Vol. 5: Finance and Awards. Pp. xv+53. (London: HMSO, 1971.) £1.37 net. [2312]

Ministry of Agriculture, Fisheries and Food—Fisheries Radiobiological Laboratory. Radioactivity in Surface and Coastal Waters of the British Isles 1970. By N. T. Mitchell. (Technical Report FRL 8.) Pp. 35. (Lowestoft: Fisheries Radiobiological Laboratory, 1971.) [2312]

Memoirs of the Royal Astronomical Society. Vol. 75, Part 3: Curves of Growth and Line Profiles for Neutral Helium Lines in Early Type Stars. By B. J. O'Mara and R. W. Simpson. Pp. 51–84. (Oxford and Edinburgh: Blackwell Scientific Publications, 1971. Published for the Royal Astronomical Society.) [2912]

X-ray Spectrometry, Vol. 1, No. 1, January 1971. Editor-in-Chief: Ron Jenkins, Westport, Conn. Pp. 1–46. Subscription price: \$25; £10; 90 DM per volume (4 issues to each volume). (London: Heyden and Son, Ltd., 1972.) [3012]

Philosophical Transactions of the Royal Society of London. A: Mathematical and Physical Sciences. Vol. 271, No. 1212 (23 December 1971): Stochastic Theory of the Nucleation of Quantized Vortices in Superfluid Helium. By R. J. Donnelly and P. H. Roberts. Pp. 41–100. (London: The Royal Society, 1971.) £1.60; \$4.15. [3112]

Other Countries

Australia: Commonwealth Scientific and Industrial Research Organization. Annual Report of the Division of Entomology, 1970–71. Pp. 115. (Canberra: CSIRO, 1971.) [912]

Rheinisch-Westfälische Akademie der Wissenschaften. Vorträge N 211. Pp. 106. (Opladen: Westdeutscher Verlag, 1971.) 16.90 DM. [912]

Comité International des Poids et Mesures. Comité Consultatif pour la Définition de la Seconde, 5^e Session—1970 (18-19 Juin). Pp. 128. (Sevres, France: Bureau International des Poids et Mesures, 1971.) [912]

Australia: Commonwealth Scientific and Industrial Research Organization. Annual Report of the Mineral Research Laboratories—Division of Mineral Chemistry and Mineralogy, 1970-71. Pp. 30. (Melbourne: CSIRO, 1971.) [912]

The African Journal of Tropical Hydrobiology and Fisheries, Vol. 1, No. 1, 1971. Pp. 1-84. Annual subscription within East Africa Sh. 35. Outside East Africa, East African Sh. 70. (Nairobi: East African Literature Bureau, 1971.) [1312]

Nederlandse Vereniging voor weer- en Sterrenkunde. Observations of Variable Stars, January-June 1971, Report No. 20. Pp. 12. (Groningen, Netherlands: Kapteyn Astronomical Laboratory, 1971.) [1312]

Australia: Commonwealth Scientific and Industrial Research Organization. Division of Soils Technical Paper No. 6: A Computer Program for Fitting Non-linear Regression Models to Data by Least Squares. By P. J. Ross. Pp. 24. (Melbourne: CSIRO, 1971.) [1312]

Annual Report of 1970 of the Keikyū Aburatsubo Marine Park Aquarium, No. 3. Pp. 71. (Miura City, Kanagawa, Japan: The Keikyū Aburatsubo Marine Park Aquarium, 1971.) [1512]

Recent Crustal Movements. (The Royal Society of New Zealand, Bulletin 9. The International Union of Geological Sciences, Series B, No. 2. Upper Mantle Project Scientific Report No. 33.) Pp. viii+247. (Wellington: The Royal Society of New Zealand, 1971.) [1512]

Australian Journal of Zoology. Supplement No. 7: The Australian Species of *Mesochra* (Crustacea: Harpacticoida) with a Comprehensive Key to the Genus. By R. Hamond. Pp. 32. (East Melbourne: Editorial and Publications Section, CSIRO, 1971.) [1612]

International Atomic Energy Agency, Vienna. Technical Report Series. No. 129: Environmental Isotope Data No. 3—World Survey of Isotope Concentration in Precipitation (1966-1967). (Report from a network organized by the IAEA in co-operation with the World Meteorological Organization and co-operating national laboratories.) Pp. xviii+399. 200 schillings; £3.33; \$8. No. 131: Rice Breeding with Induced Mutations III. (Report of an FAO/IAEA Research Co-ordination meeting on the Use of Induced Mutations in Rice Breeding, held in New Delhi, India, 22-25 September 1969.) Pp. 198. 125 schillings; £2.08; \$5. (Vienna: IAEA; London: HMSO, 1971.) [1612]

International Atomic Energy Agency. Panel Proceedings Series. Disinfestation of Fruit by Irradiation. (Proceedings of a Panel on the Use of Irradiation to Solve Quarantine Problems in the International Fruit Trade, organized by the Joint FAO/IAEA Division of Atomic Energy in Food and Agriculture, and held in Honolulu, Hawaii, 7-11 December 1970.) Pp. 177. (Vienna: IAEA; London: HMSO, 1971.) 125 schillings; £2.08; \$5. [1712]

Unesco. Science Policy Research and Teaching Units. (Science Policy Studies and Documents, No. 28.) Pp. 377. (Paris: Unesco; London: HMSO, 1971.) 20 francs; £1.50; \$5. [1712]

Light and the Universe: a Pillar of Einstein's Relativity Collapses. By Teodorico Cincin. Pp. 26. (Pescara: Accademia Teatina per le Scienze, Corso Vittorio Emanuele, 269, 1971.) [2012]

Australia: Commonwealth Scientific and Industrial Research Organization. Annual Report of the Minerals Research Laboratories, 1970-71. Pp. 30. (North Ryde, NSW: CSIRO, 1971.) [2012]

OECD at Work for Environment. Pp. 30. (Paris: Organization for Economic Co-operation and Development, 1971.) [2012]

Canada: Department of Energy, Mines and Resources. Geological Survey of Canada. Bulletin 194: Triassic Petrology of Athabasca-Smoky River Region, Alberta. By D. W. Gibson. Pp. 59 (4 plates). \$2. Bulletin 211: A Middle Ordovician Fauna from Braeside, Ottawa Valley, Ontario. By H. Miriam Steele and G. Winston Sinclair. Pp. 97 (23 plates). \$2. Paper 70-38: Miospores from the Middle and Early Upper Devonian Rocks of the Western Queen Elizabeth Islands, Arctic Archipelago. By Bernard Owens. Pp. iv+157 (28 plates). \$3.50. Paper 71-3: 1970-1971 Index of Publications of the Geological Survey of Canada. Pp. 66. \$1.50. Paper 71-36: Age of the Contact Metasomatic Copper and Iron Deposits, Vancouver and Texada Islands, British Columbia. By D. J. T. Carson, J. E. Muller, R. K. Wanless and R. D. Stevens. Pp. v+9. 75 cents. (Ottawa: Information Canada, 1971.) [2112]

Carnegie Institute of Washington. Report of the President 1970-71. Pp. 43. (Reprinted from Carnegie Institution Year Book 70 for the year 1970-71. (Washington, DC: Carnegie Institute of Washington, 1971.) [2112]

Australia: Commonwealth Scientific and Industrial Research Organization. Report of the Division of Horticultural Research 1969/71. Pp. 99. Publications List 1969-1971. Pp. 9. (Adelaide: CSIRO, 1971.) [2212]

Smithsonian Contributions to Zoology. No. 91: Systematics, Distribution, and Evolution of the *Nocomis biguttatus* Species Group (Family Cyprinidae: Pisces) with a Description of a New Species from the Ozark Upland. By Ernest A. Lachner and Robert E. Jenkins. Pp. 27. \$0.40. No. 106: Neotropical Microlepidoptera XX: Revision of the Genus *Setiostoma* (Lepidoptera: Stenomitidae). By W. Donald Duckworth. Pp. 45. (Washington, DC: Smithsonian Institution Press, 1971. For sale by US Government Printing Office.) [2312]

US Department of the Interior: Geological Survey. Professional Paper 692: Petrology of the Triassic Moenkopi Formation and Related Strata in the Colorado Plateau Region. By Robert A. Cadigan. Pp. iv+70+plate 1. (Washington, DC: Government Printing Office, 1971.) \$1.50. [2312]

Applied Mechanics Reviews. AMR Report No. 54: Cinderella (Author Index Practices and Philosophies). By S. Juhasz, M. Funnell and E. Vaught. (San Antonio, Texas: Applied Mechanics Reviews, 1971. Available from National Technical Information Service, Springfield, Va., 22151.) [2312]

World Health Organization. Technical Report Series. No. 475: WHO Expert Committee on Insecticides—Nineteenth Report. Pp. 20. 2 Sw. francs; 20p; \$0.60. No. 479: WHO Expert Committee on Yellow Fever—Third Report. Pp. 56. 3 Sw. francs; 30p; \$1. No. 480: Personal Health Care and Social Security—Report of a Joint ILO/EHO Committee. Pp. 74. 4 Sw. francs; 40p; \$1.25. No. 481: The Development of Studies in Health Manpower—Report of a WHO Scientific Group. Pp. 56. No. 483: Health Education in Health Aspects of Family Planning—Report of a WHO Study Group. Pp. 47. 3 Sw. francs; 30p; \$1. (Geneva: World Health Organization; London: HMSO, 1971.) [2912]

Background Study for the Science Council of Canada—Special Study No. 22: The Multinational Firm, Foreign Direct Investment, and Canadian Science Policy. By Arthur J. Cordell. Pp. 95. (Ottawa: Information Canada, 1971.) \$1.50. [2912]

Institut for Atomenergi, Kjeller Research Establishment. Kjeller Report No. 145: A Core Follow Study of the Dodekard Reactor with the Three-Dimensional BWR Simulator Presto. By J. Mittemberg, J. Haugen, J. Rasmussen and T. O. Saur. Pp. 21+60 figures. (Kjeller, Norway: Institut for Atomenergi, Kjeller Research Establishment, 1971.) [2912]

The Annals of Abstracting 1665-1970. Compiled by the members of the first Seminar on Abstracts and Abstracting Services, Graduate School of Library Service, University of California, Los Angeles. Edited by Robert Collison. Pp. v+54. (Los Angeles: The School of Library Service and the University Library, University of California, 1971.) \$2. [2912]

Visual Science Information Center. Visual Index, Vol. 1, No. 1, March 1971. Pp. 236. Annual Subscription Rate: \$20, USA, Canada, Mexico, \$21 other countries. (Berkeley, California: Visual Science Information Center, University of California, 1971.) [2912]

World Health Organization. Technical Report Series. No. 482: Evaluation and Testing of Drugs for Mutagenicity: Principles and Problems—Report of a WHO Scientific Group. Pp. 18. (Geneva: WHO; London: HMSO, 1971.) 2 Sw. francs; 20p; \$0.60. [3012]

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Smithsonian Contributions to Zoology. No. 106: Neotropical Microlepidoptera XX—Revision of the Genus *Setiostoma* (Lepidoptera: Stenomitidae). By W. Donald Duckworth. Pp. 45. (Washington, DC: Smithsonian Institution Press, 1971. For sale by US Government Printing Office.) 55 cents. [41]

US Department of the Interior: Geological Survey. Water-Supply Paper 1983: An Appraisal of Ground Water for Irrigation in the Wadena Area, Central Minnesota. By Gerald F. Lindholm. Pp. v+56+12 plates. (Washington, DC: Government Printing Office, 1970.) [51]

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